# Author Search

```
=> FILE HCAPLUS
FILE 'HCAPLUS' ENTERED AT 15:35:23 ON 27 DEC 2007
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PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
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FILE COVERS 1907 - 27 Dec 2007  VOL 147 ISS 26
FILE LAST UPDATED: 26 Dec 2007  (20071226/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.
'OBI' IS DEFAULT SEARCH FIELD FOR 'HCAPLUS' FILE

=> D QUE L41
L3              STR
```

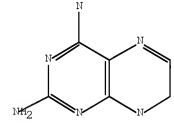

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Structure attributes must be viewed using STN Express query preparation:
Uploading strA.str
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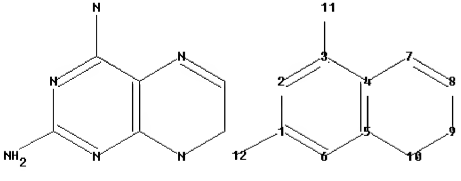


```
chain nodes :
```

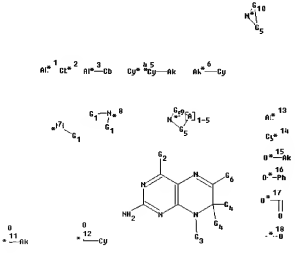
11 12
ring nodes :
1 2 3 4 5 6 7 8 9 10
chain bonds :
1-12 3-11
ring bonds :
1-2 1-6 2-3 3-4 4-5 4-7 5-6 5-10 7-8 8-9 9-10
exact/norm bonds :
1-12 3-11 4-7 5-10 7-8 8-9 9-10
normalized bonds :
1-2 1-6 2-3 3-4 4-5 5-6

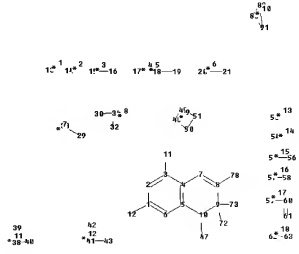
Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom
11:CLASS 12:CLASS

L5 3639 SEA FILE=REGISTRY SSS FUL L3
L32 STR

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

Structure attributes must be viewed using STN Express query preparation:
Uploading strG.str





chain nodes :
11 12 13 14 15 16 17 18 19 20 21 29 30 32 33 34 38 39 40 41 42
43 47 53 54 55 56 57 58 59 60 61 62 63 72 73 78
ring nodes :
1 2 3 4 5 6 7 8 9 10 48 49 50 51 88 89 91
chain bonds :
1-12 3-11 8-78 9-72 9-73 10-47 15-16 18-19 20-21 29-33 30-34 32-34 38-39
38-40 41-42 41-43 55-56 57-58 59-60 60-61 62-63
ring bonds :

```
1-2  1-6  2-3  3-4  4-5  4-7  5-6  5-10  7-8  8-9  9-10  48-49  48-50  49-51  50-51
88-89  88-91  89-91
exact/norm bonds :
1-12  3-11  4-7  5-10  7-8  8-9  8-78  9-10  9-72  9-73  10-47  15-16  18-19  20-21
29-33  30-34  32-34  38-39  38-40  41-42  41-43  48-49  48-50  49-51  50-51  55-56
57-58  59-60
60-61  62-63  88-89  88-91  89-91
normalized bonds :
1-2  1-6  2-3  3-4  4-5  5-6


G1:[*1],[*2],[*3],[*4],[*5],[*6]

G2:NH2,[*7],[*8],[*9],[*10]

G3:H,[*1],[*4],[*11],[*12]

G4:H,N,Cl,F,CF3,CN,[*4],[*13],[*14],[*15],[*16],[*17],[*18]

G5:C,O,S,N

G6:[*1],[*2],[*3],[*4],[*5],[*6],[*18]

Connectivity :
13:1 E exact RC ring/chain  14:1 E exact RC ring/chain  15:2 E exact RC ring/chain
16:1 E exact RC ring/chain  17:1 E exact RC ring/chain  18:2 E exact RC ring/chain
19:1 E exact
RC ring/chain  20:2 E exact RC ring/chain  21:1 E exact RC ring/chain  40:1 E exact
RC ring/chain
43:1 E exact RC ring/chain  53:1 E exact RC ring/chain  54:1 E exact RC ring/chain
56:1 E exact RC
ring/chain
Match level :
1:Atom  2:Atom  3:Atom  4:Atom  5:Atom  6:Atom  7:Atom  8:Atom  9:Atom  10:Atom
11:CLASS  12:CLASS  13:CLASS  14:Atom  15:CLASS  16:Atom  17:Atom  18:Atom
19:CLASS  20:CLASS  21:Atom
29:CLASS  30:CLASS  32:CLASS  33:CLASS  34:CLASS  38:CLASS  39:CLASS  40:CLASS
41:CLASS  42:CLASS
43:Atom  47:CLASS  48:Atom  49:Atom  50:Atom  51:Atom  53:CLASS  54:Atom  55:CLASS
56:CLASS
57:CLASS  58:CLASS  59:CLASS  60:CLASS  61:CLASS  62:CLASS  63:CLASS  72:CLASS
73:CLASS  78:CLASS
88:Atom  89:Atom  91:Atom
Generic attributes :
17:
Saturation              : Unsaturated
18:
Saturation              : Unsaturated
21:
Saturation              : Unsaturated
54:
Saturation              : Unsaturated

Element Count :
Node 13: Limited
    C,Cl-5

Node 15: Limited
    C,Cl-5
```

```
Node 19: Limited
    C,C1-5

Node 20: Limited
    C,C1-5

Node 40: Limited
    C,C1-5

Node 53: Limited
    C,C1-5

Node 56: Limited
    C,C1-5
```

```
L34          184 SEA FILE=REGISTRY SUB=L5 SSS FUL L32
L36          252 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L34
L37          220 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L36 AND (PRY<=2003 OR
                 AY<=2003 OR PY<=2003)
L38            4 SEA FILE=HCAPLUS ABB=ON  PLU=ON  DOBLHOFER R?/AU
L39           56 SEA FILE=HCAPLUS ABB=ON  PLU=ON  TEGTMEIER F?/AU
L40           57 SEA FILE=HCAPLUS ABB=ON  PLU=ON  (L38 OR L39)
L41            3 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L40 AND L37
```

```
=> D QUE L48
L3              STR
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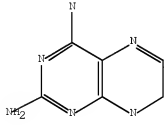


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Structure attributes must be viewed using STN Express query preparation:
Uploading strH.str
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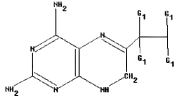
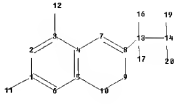




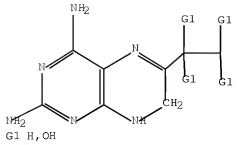
```
chain nodes :
11  12  13  14  16  17  19  20
ring nodes :
1  2  3  4  5  6  7  8  9  10
chain bonds :
1-11  3-12  8-13  13-14  13-16  13-17  14-19  14-20
ring bonds :
1-2  1-6  2-3  3-4  4-5  4-7  5-6  5-10  7-8  8-9  9-10
exact/norm bonds :
1-11  3-12  4-7  5-10  7-8  8-9  9-10  13-16  13-17  14-19  14-20
exact bonds :
8-13  13-14
normalized bonds :
1-2  1-6  2-3  3-4  4-5  5-6

G1:H,OH

Match level :
1:Atom  2:Atom  3:Atom  4:Atom  5:Atom  6:Atom  7:Atom  8:Atom  9:Atom  10:Atom
11:CLASS  12:CLASS  13:CLASS  14:CLASS  16:CLASS  17:CLASS  19:CLASS  20:CLASS



L5          3639 SEA FILE=REGISTRY SSS FUL L3
L38            4 SEA FILE=HCAPLUS ABB=ON  PLU=ON  DOBLHOFER R?/AU
L39           56 SEA FILE=HCAPLUS ABB=ON  PLU=ON  TEGTMEIER F?/AU
L40           57 SEA FILE=HCAPLUS ABB=ON  PLU=ON  (L38 OR L39)
L42              STR
```




```
Structure attributes must be viewed using STN Express query preparation.
L45             7 SEA FILE=REGISTRY SUB=L5 SSS FUL L42
L46             9 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L45
L47             7 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L46 AND (PRY<=2003 OR
                  AY<=2003 OR PY<=2003)
L48             2 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L40 AND L47


=> FILE WPIX
FILE 'WPIX' ENTERED AT 15:35:46 ON 27 DEC 2007
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FILE LAST UPDATED:                          21 DEC 2007   <20071221/UP>
MOST RECENT THOMSON SCIENTIFIC UPDATE:     200782      <200782/DW>
DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE

>>> IPC Reform backfile reclassification has been loaded to September 6th
    2007. No update date (UP) has been created for the reclassified
    documents, but they can be identified by 20060101/UPIC and
    20061231/UPIC, 20070601/UPIC and 20071001/UPIC. <<<

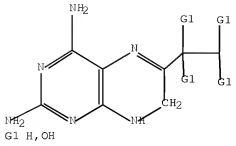

FOR A COPY OF THE DERWENT WORLD PATENTS INDEX STN USER GUIDE,
PLEASE VISIT:
http://www.stn-international.de/training_center/patents/stn_guide.pdf

FOR DETAILS OF THE PATENTS COVERED IN CURRENT UPDATES, SEE
http://scientific.thomson.com/support/patents/coverage/latestupdates/

EXPLORE DERWENT WORLD PATENTS INDEX IN STN ANAVIST, VERSION 2.0:
http://www.stn-international.com/archive/presentations/DWPIAnaVist2_0710.pdf

 >>> XML document distribution format now available.
                                    See HELP XMLDOC <<<
'BI,ABEX' IS DEFAULT SEARCH FIELD FOR 'WPIX' FILE

=> D QUE L52
L38             4 SEA FILE=HCAPLUS ABB=ON  PLU=ON  DOBLHOFER R?/AU
L39            56 SEA FILE=HCAPLUS ABB=ON  PLU=ON  TEGTMEIER F?/AU
L40            57 SEA FILE=HCAPLUS ABB=ON  PLU=ON  (L38 OR L39)
L42                STR
```

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Structure attributes must be viewed using STN Express query preparation.
L50             1 SEA FILE=WPIX SSS FUL L42
L51             2 SEA FILE=WPIX ABB=ON  PLU=ON  L50/DCR
L52             0 SEA FILE=WPIX ABB=ON  PLU=ON  L40 AND L51


=> DUP REM L52 L41 L48
L52 HAS NO ANSWERS
FILE 'HCAPLUS' ENTERED AT 15:36:00 ON 27 DEC 2007
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FILE COVERS 1907 - 27 Dec 2007  VOL 147 ISS 26
FILE LAST UPDATED: 26 Dec 2007  (20071226/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.
'OBI' IS DEFAULT SEARCH FIELD FOR 'HCAPLUS' FILE
PROCESSING COMPLETED FOR L52
PROCESSING COMPLETED FOR L41
PROCESSING COMPLETED FOR L48
L58             3 DUP REM L52 L41 L48 (2 DUPLICATES REMOVED)
                  ANSWERS '1-3' FROM FILE HCAPLUS

=> D IBIB ED ABS HITSTR L58 1-3

L58  ANSWER 1 OF 3  HCAPLUS  COPYRIGHT 2007 ACS on STN DUPLICATE 1
ACCESSION NUMBER:         2005:371070  HCAPLUS  Full-text
DOCUMENT NUMBER:          142:404279
TITLE:                    Use of pteridine derivatives for the treatment of
                          increased intracranial pressure and secondary ischemia
```
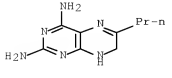
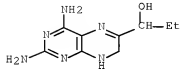

INVENTOR(S): Doblhofer, Robert; Tegtmeier, Frank
PATENT ASSIGNEE(S): Vasopharm Biotech GmbH, Germany
SOURCE: PCT Int. Appl., 41 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2005037286 | A1 | 20050428 | WO 2003-EP3096 | 20030325 <-- |
| W: US | | | | |
| CA 2519919 | A1 | 20041007 | CA 2003-2519919 | 20031008 <-- |
| WO 2004084906 | A1 | 20041007 | WO 2003-EP11138 | 20031008 <-- |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| AU 2003293607 | A1 | 20041018 | AU 2003-293607 | 20031008 <-- |
| EP 1605947 | A1 | 20051221 | EP 2003-788945 | 20031008 <-- |
| EP 1605947 | B1 | 20060802 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK | | | | |
| CN 1758913 | A | 20060412 | CN 2003-80110211 | 20031008 <-- |
| JP 2006514965 | T | 20060518 | JP 2004-569858 | 20031008 <-- |
| AT 334681 | T | 20060815 | AT 2003-788945 | 20031008 <-- |
| ES 2270151 | T3 | 20070401 | ES 2003-3788945 | 20031008 <-- |
| MX 2005PA09491 | A | 20060222 | MX 2005-PA9491 | 20050906 <-- |
| US 2007032498 | A1 | 20070208 | US 2006-549200 | 20060703 <-- |
| PRIORITY APPLN. INFO.: | | | WO 2003-EP3096 A | 20030325 <-- |
| | | | WO 2003-EP11138 W | 20031008 <-- |

OTHER SOURCE(S): MARPAT 142:404279
ED Entered STN: 29 Apr 2005
AB The invention discloses the use of pteridine derivs. for treating increased intracranial pressure and/or secondary ischemia. Compound preparation is included.
IT 50691-64-0 767288-02-8
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pteridine derivs. for treatment of increased intracranial pressure and secondary ischemia)
RN 50691-64-0 HCAPLUS
CN 2,4-Pteridinediamine, 1,7-dihydro-6-propyl- (9CI) (CA INDEX NAME)

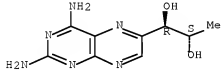


RN 767288-02-8 HCAPLUS
CN 6-Pteridinemethanol, 2,4-diamino-α-ethyl-1,7-dihydro- (9CI) (CA INDEX NAME)



IT 13535-20-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(pteridine derivs. for treatment of increased intracranial pressure and secondary ischemia)
RN 13535-20-1 HCAPLUS
CN 1,2-Propanediol, 1-(2,4-diamino-6-pteridinyl)-, (1R,2S)- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L58 ANSWER 2 OF 3 HCAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 2
ACCESSION NUMBER: 2004:817714 HCAPLUS Full-text
DOCUMENT NUMBER: 141:307610
TITLE: Use of pteridine derivatives for the treatment of increased intracranial pressure, secondary ischemia, and disorders associated with an increased level of cytotoxic reactive oxygen species
INVENTOR(S): Doblhofer, Robert; Tegtmeier, Frank
PATENT ASSIGNEE(S): Vasopharm Biotech G.m.b.H., Germany
SOURCE: PCT Int. Appl., 47 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2004084906 | A1 | 20041007 | WO 2003-EP11138 | 20031008 <-- |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, | | | | |

LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ,
OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM,
TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,
BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

| | | | | | | |
|---|---|---|---|---|---|---|
| WO 2005037286 | | A1 | 20050428 | WO 2003-EP3096 | 20030325 | <-- |
| W: US | | | | | | |
| CA 2519919 | | A1 | 20041007 | CA 2003-2519919 | 20031008 | <-- |
| AU 2003293607 | | A1 | 20041018 | AU 2003-293607 | 20031008 | <-- |
| EP 1605947 | | A1 | 20051221 | EP 2003-788945 | 20031008 | <-- |
| EP 1605947 | | B1 | 20060802 | | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, | | | | | | |
| IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK | | | | | | |
| JP 2006514965 | | T | 20060518 | JP 2004-569858 | 20031008 | <-- |
| MX 2005PA09491 | | A | 20060222 | MX 2005-PA9491 | 20050906 | <-- |
| US 2007032498 | | A1 | 20070208 | US 2006-549200 | 20060703 | <-- |
| PRIORITY APPLN. INFO.: | | | | WO 2003-EP3096 | A 20030325 | <-- |
| | | | | WO 2003-EP11138 | W 20031008 | <-- |

OTHER SOURCE(S): MARPAT 141:307610

ED Entered STN: 07 Oct 2004

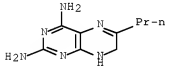
AB The present invention relates to the use of pteridine derivs. for the treatment of increased intracranial pressure, secondary ischemia, and disorders associated with an increased level of cytotoxic reactive oxygen species. H4-aminobiopterin (preparation given) caused a clear concentration dependent contraction of both rat basilar arteries and middle cerebral arteries.

IT 50691-64-0 767288-02-8

RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pteridine derivs. for treatment of increased intracranial pressure, secondary ischemia, and disorders associated with increased levels of cytotoxic reactive oxygen species)

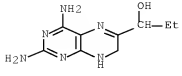
RN 50691-64-0 HCAPLUS

CN 2,4-Pteridinediamine, 1,7-dihydro-6-propyl- (9CI) (CA INDEX NAME)



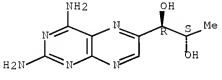

RN 767288-02-8 HCAPLUS

CN 6-Pteridinemethanol, 2,4-diamino-α-ethyl-1,7-dihydro- (9CI) (CA INDEX NAME)



IT 13535-20-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(pteridine derivs. for treatment of increased intracranial pressure, secondary ischemia, and disorders associated with increased levels of cytotoxic reactive oxygen species)
RN 13535-20-1 HCAPLUS
CN 1,2-Propanediol, 1-(2,4-diamino-6-pteridinyl)-, (1R,2S)- (CA INDEX NAME)

Absolute stereochemistry.




REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L58 ANSWER 3 OF 3 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:612291 HCAPLUS Full-text
DOCUMENT NUMBER: 143:153229
TITLE: Preparation of pharmaceutical compositions containing 4-amino-7,8-dihydropteridines and their use for the treatment of diseases which are caused by an increased nitric oxide level
INVENTOR(S): Doblhofer, Robert; Tegtmeier, Frank
PATENT ASSIGNEE(S): Vasopharm Biotech G.m.b.H., Germany
SOURCE: PCT Int. Appl., 46 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2005063752 | A1 | 20050714 | WO 2003-EP14970 | 20031230 <-- |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| CA 2552195 | A1 | 20050714 | CA 2003-2552195 | 20031230 <-- |
| AU 2003290127 | A1 | 20050721 | AU 2003-290127 | 20031230 <-- |
| EP 1699793 | A1 | 20060913 | EP 2003-782489 | 20031230 <-- |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, SK | | | | |
| JP 2007525407 | T | 20070906 | JP 2005-512684 | 20031230 <-- |

IN 2006DN03444 A 20070831 IN 2006-DN3444 20060615 <--
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OTHER SOURCE(S): MARPAT 143:153229
ED Entered STN: 15 Jul 2005
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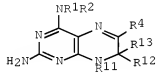

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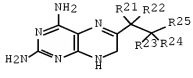

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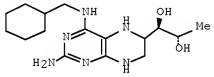

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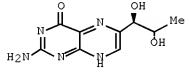


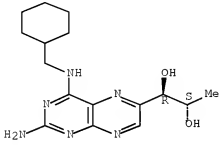
IV

AB The present invention relates to the area of NO synthase inhibition and, more particularly, relates to novel 4-amino-7,8-dihydropteridines, e.g., I [R1, R2 = H, C1-20-alkyl, C1-20-alkenyl, C1-20-alkynyl, C3-8-cycloalkyl, cycloalkenyl, (cycloalkyl)alkyl, aryl, (c1-3-alkyl)aryl, etc.; NR1R2 = 3- to 8-membered ring (optionally containing 1 or 2 other heteroatoms - O, S, N); R4 = C1-20-alkyl, C1-20-alkenyl, C1-20-alkynyl, C3-8-cycloalkyl, cycloalkenyl, (cycloalkyl)alkyl, aryl, (C1-3-alkyl)aryl, etc.; R6, R7 = F, Cl, I, Br, O-(C1-10-alkyl), OPh, OC(:O)(C1-10-alkyl), OC(:O)aryl, NR8R9, oxo, Ph, C(:O)(C1-5-alkyl), CF3, CN, CONR8R9, CO2H, C(:O)O-(C1-5-alkyl), C(:O)O-aryl, S(O)n-(C1-5-alkyl), SO2NR8R9; R8 = H, C1-20-alkyl; R9 = H, C1-20-alkyl, aryl (preferably Ph); R11 = H, C1-20-alkyl, aryl, CO-alkyl, CO-aryl; R12, R13 = H, C1-10-alkyl, aryl, O-(C1-10-alkyl), OPh, OC(:O)-C1-10-alkyl, OC(:O)-aryl, NR8R9, Ph, C(:O)-C1-10-alkyl, CF3, CN, CONR8R9, CO2H, etc.; aryl = (un)substituted Ph, naphthyl, heteroaryl; heteroaryl = 5- to 7-membered ring (optionally containing an addnl. heteroatom - O, N, S); n = 0 - 2], or their pharmaceutically acceptable acid addition salts, hydrates and esters, pharmaceutical compns. containing said compds., and the use of said compds. in the treatment of a disorder characterized by a disturbed nitric oxide level. The patent particularly excludes compds. II [R21, R22, R23, R24 = ; R25 = H, Me, CH2OH, CHO, (un)branched C1-9-alkyl, (CHOH)nY, (CHOH)n(CH2)mW; Y = H, C1-9-alkyl; W = H, OH; n, m = 1 - 20]. Thus, 4-[(Cyclohexylmethyl)amino]-5,6,7,8-tetrahydrobiopterin (III) was prepared from biopterin (IV) via acetylation with Ac2O in pyridine, reaction with PhCH2CH2OH in dioxane containing Ph3P, amination with (cyclohexylmethyl)amine in dioxane, and hydrogenation in CF2CO4H containing catalytic PtO2. The in vivo stability [t1/2 = << 5 min. (tetrahydro); t1/2 = 48 min. (dihydro)] and NO release inhibitor activity for I was determined

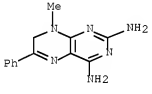
IT 858127-61-4P, N4-[(Cyclohexylmethyl)amino]-4-desoxy-L-biopterin
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and hydrogenation of; preparation of pharmaceutical compns.

containing
4-amino-7,8-dihydropteridines and their use for the treatment of diseases which are caused by an increased nitric oxide level)
RN 858127-61-4 HCAPLUS
CN 1,2-Propanediol, 1-[2-amino-4-[(cyclohexylmethyl)amino]-6-pteridinyl]-, (1R,2S)- (CA INDEX NAME)

Absolute stereochemistry.



IT 858127-54-5P, 2,4-Diamino-8-methyl-6-phenyl-7,8-dihydropteridine
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of pharmaceutical compns. containing 4-amino-7,8-dihydropteridines
and their use for the treatment of diseases which are caused by an increased nitric oxide level)
RN 858127-54-5 HCAPLUS
CN 2,4-Pteridinediamine, 7,8-dihydro-8-methyl-6-phenyl- (CA INDEX NAME)



REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

# Structure Search

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```



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FILE COVERS 1907 - 27 Dec 2007  VOL 147 ISS 26
FILE LAST UPDATED: 26 Dec 2007  (20071226/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.
'OBI' IS DEFAULT SEARCH FIELD FOR 'HCAPLUS' FILE

=> D QUE L47
L3              STR
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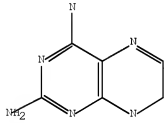


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L42             STR
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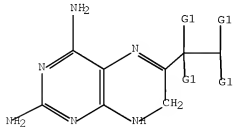

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Structure attributes must be viewed using STN Express query preparation.
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L46           9 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L45
L47           7 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L46 AND (PRY<=2003 OR
                AY<=2003 OR PY<=2003)


=> S L47 NOT L41,L48
L59           5 L47 NOT (L41 OR L48)

=> FILE WPIX
FILE 'WPIX' ENTERED AT 15:36:48 ON 27 DEC 2007
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FILE LAST UPDATED:                          21 DEC 2007   <20071221/UP>
MOST RECENT THOMSON SCIENTIFIC UPDATE:     200782      <200782/DW>
DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE

>>> IPC Reform backfile reclassification has been loaded to September 6th
    2007. No update date (UP) has been created for the reclassified
    documents, but they can be identified by 20060101/UPIC and
    20061231/UPIC, 20070601/UPIC and 20071001/UPIC. <<<


FOR A COPY OF THE DERWENT WORLD PATENTS INDEX STN USER GUIDE,
PLEASE VISIT:
http://www.stn-international.de/training_center/patents/stn_guide.pdf

FOR DETAILS OF THE PATENTS COVERED IN CURRENT UPDATES, SEE
http://scientific.thomson.com/support/patents/coverage/latestupdates/

EXPLORE DERWENT WORLD PATENTS INDEX IN STN ANAVIST, VERSION 2.0:
http://www.stn-international.com/archive/presentations/DWPIAnaVist2_0710.pdf

 >>> XML document distribution format now available.
                                          See HELP XMLDOC <<<
'BI,ABEX' IS DEFAULT SEARCH FIELD FOR 'WPIX' FILE

=> D QUE L51
L42             STR
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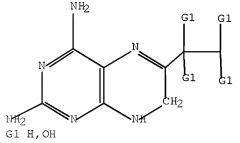


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Structure attributes must be viewed using STN Express query preparation.
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=> S L51 NOT L52
L60             2 L51 NOT L52

=> FILE BEILSTEIN
FILE 'BEILSTEIN' ENTERED AT 15:37:07 ON 27 DEC 2007
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FILE LAST UPDATED ON September 26, 2007

FILE COVERS 1771 TO 2007.
*** FILE CONTAINS 10.119,480  SUBSTANCES ***

>>>PLEASE NOTE: Reaction Data and substance data are stored in
   separate documents and can not be searched together in one query.
   Reaction data for BEILSTEIN compounds may be displayed
   immediately with the display codes PRE (preparations) and REA
   (reactions).  A substance answer set retrieved after the search
   for a chemical name, a compounds with available reaction
   information by combining with PRE/FA, REA/FA or more generally
   with RX/FA. The BEILSTEIN Registry Number (BRN) is the link
   between a BEILSTEIN compound and belonging reactions. For mo
   detailed reaction searches BRNs can be searched as reaction
   partner BRNs Reactant BRN (RX.RBRN) or Product BRN (RX.PBRN).<<<

>>> FOR SEARCHING PREPARATIONS SEE HELP PRE  <<<

*********************************************************************
* PLEASE NOTE THAT THERE ARE NO FORMATS FREE OF COST.               *
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* ARE BASED ON THE HIGHEST PRICE CATEGORY. THEREFORE; THESE         *
* ESTIMATES MAY NOT REFLECT THE ACTUAL COSTS.                       *
* FOR PRICE INFORMATION SEE HELP COST                               *
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>>> Price change as of January 1st, 2008: Connect Time and Structure
    Search fees re-introduced. See NEWS and HELP COST <<<

=> D QUE L53
L3              STR
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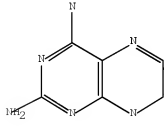


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Structure attributes must be viewed using STN Express query preparation.
L5          3639 SEA FILE=REGISTRY SSS FUL L3
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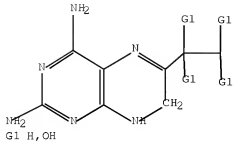
L42 STR




Structure attributes must be viewed using STN Express query preparation.
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L53 3 SEA FILE=BEILSTEIN ABB=ON PLU=ON L45

=> FILE MARPAT
FILE 'MARPAT' ENTERED AT 15:37:14 ON 27 DEC 2007
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FILE CONTENT: 1961-PRESENT VOL 147 ISS 26 (20071221/ED)

SOME MARPAT RECORDS ARE DERIVED FROM INPI DATA FOR 1961-1987

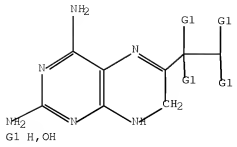
MOST RECENT CITATIONS FOR PATENTS FROM MAJOR ISSUING AGENCIES
(COVERAGE TO THESE DATES IS NOT COMPLETE):

US 2007270387 22 NOV 2007
DE 102007020009 31 OCT 2007
EP 1849853 31 OCT 2007
JP 2007294323 08 NOV 2007
WO 2007129745 15 NOV 2007
GB 2437429 24 OCT 2007
FR 2900574 09 NOV 2007
RU 2309952 10 NOV 2007
CA 2584745 13 OCT 2007

Expanded G-group definition display now available.

Effective December 15th the iteration and answer limits in MARPAT
have increased from 100,000 to 200,000 for both on-line and batch
searches. For more information on MARPAT search limits, type HELP
SLIMITS at an arrow prompt.

=> D QUE L57
L42 STR

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L57           13 SEA FILE=MARPAT ABB=ON  PLU=ON  L56/COM


=> DUP REM L59 L60 L53 L57
DUPLICATE IS NOT AVAILABLE IN 'BEILSTEIN'.
ANSWERS FROM THESE FILES WILL BE CONSIDERED UNIQUE
FILE 'HCAPLUS' ENTERED AT 15:37:44 ON 27 DEC 2007
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PROCESSING COMPLETED FOR L59
PROCESSING COMPLETED FOR L60
PROCESSING COMPLETED FOR L53
PROCESSING COMPLETED FOR L57
L61           20 DUP REM L59 L60 L53 L57 (3 DUPLICATES REMOVED)
                 ANSWERS '1-5' FROM FILE HCAPLUS
                 ANSWER '6' FROM FILE WPIX
                 ANSWERS '7-9' FROM FILE BEILSTEIN
                 ANSWERS '10-20' FROM FILE MARPAT

=> D IBIB ED ABS HITSTR L61 1-5; D IBIB AB HITSTR L61 6; D IDE ALLREF 7-9; D IBIB
AB QHIT L61 10-20

L61  ANSWER 1 OF 20  HCAPLUS  COPYRIGHT 2007 ACS on STN DUPLICATE 1
ACCESSION NUMBER:         1999:236988  HCAPLUS  Full-text
DOCUMENT NUMBER:          130:276776
TITLE:                    Pteridine derivatives as NO synthase inhibitors
INVENTOR(S):              Werner, Ernst; Schircks, Bernhard
PATENT ASSIGNEE(S):       Austria
SOURCE:                   Eur. Pat. Appl., 7 pp.
                          CODEN: EPXXDW
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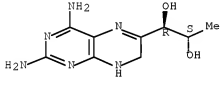
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| EP 906913 | A1 | 19990407 | EP 1997-117276 | 19971006 <-- |
| EP 906913 | B1 | 20010523 | | |

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO

PRIORITY APPLN. INFO.: EP 1997-117276 19971006 <--
OTHER SOURCE(S): MARPAT 130:276776
ED Entered STN: 19 Apr 1999
AB Pteridine derivs. such as dihydroaminobiopterin are useful as NO synthase inhibitors. Thus, 2,4-diamino-6-(L-erythro-1,2-dihydroxypropyl)pteridine was reduced with Na2S2O4 to give the 7,8-dihydro compound The effectiveness of the compound in inhibiting the enzyme was demonstrated.
IT 222420-39-5P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(pteridine derivs. as NO synthase inhibitors)
RN 222420-39-5 HCAPLUS
CN 1,2-Propanediol, 1-(2,4-diamino-1,7-dihydro-6-pteridinyl)-, (1R,2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.




REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L61 ANSWER 2 OF 20 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1988:112955 HCAPLUS Full-text
DOCUMENT NUMBER: 108:112955
TITLE: Preparation of diastereomers of 10-alkyl-10-deazaminopterins as neoplasm inhibitors
INVENTOR(S): DeGraw, Joseph I.; Christie, Pamela H.; Sirotnak, Francis M.
PATENT ASSIGNEE(S): SRI International, USA; Memorial Sloan Kettering Cancer Center
SOURCE: PCT Int. Appl., 26 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 8704161 | A1 | 19870716 | WO 1986-US2513 | 19861124 <-- |

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        W:  DE, GB, JP
        RW: FR
     US 4746659          A     19880524    US 1985-814720          19851230 <--
     DE 3690639          T0    19871119    DE 1986-3690639         19861124 <--
     GB 2192888          A     19880127    GB 1987-18482           19861124 <--
     GB 2192888          B     19891018
     EP 254726           A1    19880203    EP 1986-907213          19861124 <--
        R:  FR
     JP 63502892         T     19881027    JP 1986-506186          19861124 <--
     JP 08009619         B     19960131
PRIORITY APPLN. INFO.:                      US 1985-814720      A   19851230 <--
                                            WO 1986-US2513      W   19861124 <--
OTHER SOURCE(S):         CASREACT 108:112955; MARPAT 108:112955
ED   Entered STN:  01 Apr 1988
GI
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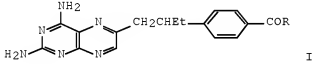


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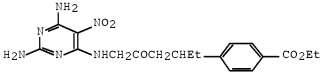



IV

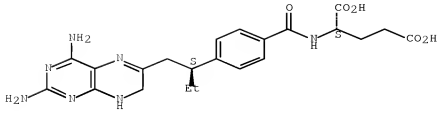
AB The title compds. I [R = NHCH(CO2H)CH2CH2CO2H; 1 of R1, R2 = C1-8 alkyl and the other = H, C1-8 alkyl; R1 ≠ R2] were prepared as neoplasm inhibitors in a 14-step synthesis. 4-PrC6H4CO2H was added to LDA in THF followed by H2C:CHCH2Br to give, after esterification, 63% 4-(MeO2C)C6H4CHEtCH2CH:CH2 which was stirred 30 min with NaIO4 and RuO2 to give 77% 4-(MeO2C)C6H4CHEtCH2CO2H. Resolution with (+)-PhCHMeNH2 was accomplished at this stage. (Pyrimidinylamino)hexanone IV (produced in 7 addnl. steps) was stirred at 90-100° in AcOH containing Zn dust to give 83% I (R = Et). D,L-10-Ethyl-10-deazaminopterin (II), at 12 mg/kg i.p., increased survival time of mice inoculated with L1210 cells by 200% over controls. Tablets were prepared each containing II 15, lactose 86, starch 45.5, gelatin 2.5, and Mg stearate 1.0 mg.

IT 102153-04-8P 102153-05-9P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of, as neoplasm inhibitor)

RN 102153-04-8 HCAPLUS

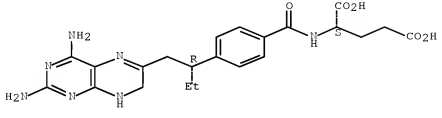
CN L-Glutamic acid, N-[4-[1-[(2,4-diamino-1,7-dihydro-6-pteridinyl)methyl]propyl]benzoyl]-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

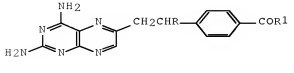


RN 102153-05-9 HCAPLUS
CN L-Glutamic acid, N-[4-[1-[(2,4-diamino-1,7-dihydro-6-pteridinyl)methyl]propyl]benzoyl]-, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L61 ANSWER 3 OF 20 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1986:424246 HCAPLUS Full-text
DOCUMENT NUMBER: 105:24246
TITLE: Synthesis and biological activity of resolved carbon-10 diastereomers of 10-methyl- and 10-ethyl-10-deazaminopterin
AUTHOR(S): DeGraw, J. I.; Christie, P. H.; Tagawa, H.; Kisliuk, R. L.; Gaumont, Y.; Schmid, F. A.; Sirotnak, F. M.
CORPORATE SOURCE: Bio-Org. Chem. Lab., SRI Int., Menlo Park, CA, 94025, USA
SOURCE: Journal of Medicinal Chemistry (1986), 29(6), 1056-61
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 105:24246
ED Entered STN: 26 Jul 1986
GI



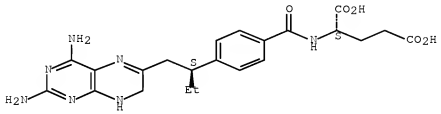
I

AB Aminodeoxydeazapteroic acids I (R = Me, Et, R1 = OH) were prepared and coupled with L-glutamate to afford the appropriate diastereomers of the title compds. [I; R1 = Glu) (II)]. Biochem., transport, and cell growth inhibitory properties in L1210 cells and folate-dependent bacteria were measured. Differences were generally less than 2-fold between diastereomeric pairs, but a factor of 3 was noted for d,L-II (R = Et) vs. the l,L diastereomer in inhibition of DHFR from L1210 cells and in cytotoxicity toward L1210 cells. An in vivo comparison of the isomers of II (R = Et) with racemic compound against L1210 in mice did not show a significant efficacy difference among the compds. However, d,L-II (R = Et) showed an acute toxicity about 2.5 times that of l,L-II (R = Et).

IT 102153-04-8P 102153-05-9P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation and antibacterial and antitumor activity of)

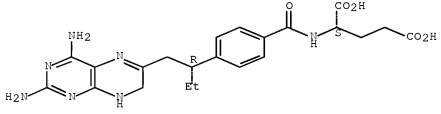
RN 102153-04-8 HCAPLUS
CN L-Glutamic acid, N-[4-[1-[(2,4-diamino-1,7-dihydro-6-pteridinyl)methyl]propyl]benzoyl]-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 102153-05-9 HCAPLUS
CN L-Glutamic acid, N-[4-[1-[(2,4-diamino-1,7-dihydro-6-pteridinyl)methyl]propyl]benzoyl]-, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L61 ANSWER 4 OF 20 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1985:221167 HCAPLUS Full-text
DOCUMENT NUMBER: 102:221167
ORIGINAL REFERENCE NO.: 102:34715a,34718a
TITLE: Folate analogs. 24. Syntheses of the antitumor agents 10-deazaaminopterin (10-DAAM) and 10-ethyl-10-deazaaminopterin (10-EDAAM)
AUTHOR(S): Nair, M. G.

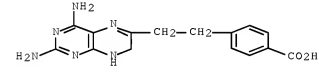
CORPORATE SOURCE: Coll. Med., Univ. South Alabama, Mobile, AL, 36688, USA
SOURCE: Journal of Organic Chemistry (1985), 50(11), 1879-84
CODEN: JOCEAH; ISSN: 0022-3263
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 102:221167
ED Entered STN: 29 Jun 1985
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

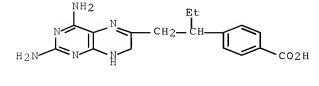
AB Title folate analogs I (R = H and Et, resp.) were prepared by condensing pteroic acids II with di-Et glutamate by ClCO2CH2CHMe3 and saponifying the resulting di-Et esters of I. Phthalimide III (R1 = CH2Br) was treated with Ph3P to give the corresponding phosphonium bromide, which was treated with NaOMe in DMF to give Wittig reagent III (R1 = CH:PPh3), which was treated with p-MeO2CC6H4CHO to give enone III (R1 = CH:CHC6H4CO2Me-p) (IV). IV was reduced by Zn/HOAc to give ketone V (R = H), whereas IV was treated with EtMgBr to give V (R = Et). V (R = H, Et) were converted to oximes VI, which was treated with 6-chloro-2,4-diamino-5-nitropyrimidine to give pyrimidines VII, which were converted to II (R = N, Et) by multistep procedures.

IT 96056-44-9P 96056-45-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and oxidation of)

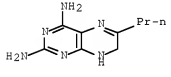
RN 96056-44-9 HCAPLUS
CN Benzoic acid, 4-[2-(2,4-diamino-1,7-dihydro-6-pteridinyl)ethyl]- (9CI) (CA INDEX NAME)



RN 96056-45-0 HCAPLUS
CN Benzoic acid, 4-[1-[(2,4-diamino-1,7-dihydro-6-pteridinyl)methyl]propyl]- (9CI) (CA INDEX NAME)



L61 ANSWER 5 OF 20 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1973:537092 HCAPLUS Full-text
DOCUMENT NUMBER: 79:137092
ORIGINAL REFERENCE NO.: 79:22221a,22224a
TITLE: Pteridines. XXIX. Unequivocal route to 2,4-diamino-6-substituted pteridines
AUTHOR(S): Taylor, Edward C.; Perlman, Katherine L.; Kim, Young-Ho; Sword, Ian P.; Jacobi, Peter A.
CORPORATE SOURCE: Dep. Chem., Princeton Univ., Princeton, NJ, USA
SOURCE: Journal of the American Chemical Society (1973), 95(19), 6413-18
CODEN: JACSAT; ISSN: 0002-7863
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 12 May 1984
GI For diagram(s), see printed CA Issue.
AB 2,4-Diamino-6-substituted pteridines (I) are prepared Reaction of an α-keto-aldoxime with aminomalononitrile gives 2-amino-3-cyano-5- substituted pyrazine 1-oxides which yield 2,4-diamino-6-substituted pteridine 8-oxides upon cyclization with guanidine. 2,4-Diaminopteridines are then obtained by deoxygenation of the corresponding 8-oxides, or alternately by prior deoxygenation of these pyrazine 1-oxides, followed by cyclization with guanidine. The conversion of 2-amino-3-cyano-5- methylpyrazine 1-oxide to the corresponding 1,4-dioxide, and a number of chemical transformations of this latter intermediate, are also described.
IT 50691-64-0P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 50691-64-0 HCAPLUS
CN 2,4-Pteridinediamine, 1,7-dihydro-6-propyl- (9CI) (CA INDEX NAME)




L61 ANSWER 6 OF 20 WPIX COPYRIGHT 2007 THE THOMSON CORP on STN
DUPLICATE 2
ACCESSION NUMBER: 1999-404476 [34] WPIX
DOC. NO. CPI: C1999-119322 [34]
TITLE: New and known pteridine derivatives are nitric oxide synthase inhibitors useful for the treatment of Parkinson's disease, Alzheimer's disease, septic shock and asthma
DERWENT CLASS: B02
INVENTOR: WERNER E
PATENT ASSIGNEE: (WERN-I) WERNER E
COUNTRY COUNT: 1

PATENT INFO ABBR.:

| PATENT NO | KIND | DATE | WEEK | LA | PG | MAIN IPC |
|---|---|---|---|---|---|---|
| US 5922713 | A | 19990713 | (199934)* | EN | 7[0] | |

APPLICATION DETAILS:

| PATENT NO | KIND | APPLICATION | DATE |
|---|---|---|---|
| US 5922713 A | | US 1997-882456 | 19970626 |

PRIORITY APPLN. INFO: US 1997-882456 19970626

AB US 5922713 A UPAB: 20050521

NOVELTY - Pteridine derivatives (I) and their salts are used as nitric oxide synthase inhibitors to inhibit nitric oxide synthesis in an organism.

DETAILED DESCRIPTION - The use of pteridine derivatives of formula (I) or their salts to inhibit nitric oxide synthase and nitric oxide synthesis in an organism, is new.

Z = CH(OH)X;

X = CH(OH)CH3, (CH(OH))nY or (CH(OH))n(CH2)nW;

Y = H or lower alkyl;

W = H or OH;

n = 1-20; and

a, b = single or double bonds.

An INDEPENDENT CLAIM is also included stating that (I) are new, provided that when a and b are both double bonds, Z is not (CH(OH))2CH3, (CH(OH))2CH2OH or ((CH(OH))3CH2OH.

ACTIVITY - Antiparkinsonian; nootropic; neuroprotective; antibacterial; immunosuppressive; antiasthmatic.

MECHANISM OF ACTION - Nitric oxide synthase inhibitor.

The method of Mayer et al. (Neuropharmacology, 33, 1253-1259, 1994) was used to measure inhibition of recombinant rat neuronal nitric oxide synthase. Tetrahydroaminobiopterin of formula (Ia) at a concentration of 30 microM inhibited nitric oxide synthase activity by 83%, compared to the known compound 2,4-diamino-5,6,7,8-tetrahydro-6-hydroxymethyl pteridine which gave inhibition of 4% at the same concentration.

USE - As nitric oxide synthase inhibitors (claimed) for the treatment of neurodegenerative diseases such as Parkinson's disease and Alzheimer's disease, septic shock and asthma.

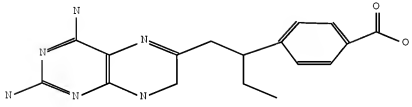
ADVANTAGE - The 5,6,7,8-tetrahydro-L-erythrobiopterin (tetrahydrobiopterin) moiety tightly binds nitric oxide synthase and provides better inhibition of nitric oxide synthase than prior art compounds.

L61 ANSWER 7 OF 20 BEILSTEIN COPYRIGHT 2007 BEILSTEIN MDL on STN

| | |
|---|---|
| Beilstein Records (BRN): | 5633531 |
| Beilstein Pref. RN (BPR): | 96056-45-0 |
| CAS Reg. No. (RN): | 96056-45-0 |
| Chemical Name (CN): | 4-<1-(2,4-diamino-7,8-dihydro-pteridin-6-ylmethyl)-propyl>-benzoic acid |
| Autonom Name (AUN): | 4-<1-(2,4-diamino-7,8-dihydro-pteridin-6- |

ylmethyl)-propyl>-benzoic acid

| | |
|---|---|
| Molec. Formula (MF): | C17 H20 N6 O2 |
| Molecular Weight (MW): | 340.38 |
| Lawson Number (LN): | 30750 |
| Compound Type (CTYPE): | heterocyclic |
| Constitution ID (CONSID): | 4970420 |
| Tautomer ID (TAUTID): | 5406500 |
| Beilstein Citation (BSO): | 6-26 |
| Entry Date (DED): | 1993/02/12 |
| Update Date (DUPD): | 1994/02/18 |



Field Availability:

| Code | Name | Occurrence |
|---|---|---|
| BRN | Beilstein Records | 1 |
| BPR | Beilstein Preferred RN | 1 |
| RN | CAS Registry Number | 1 |
| CN | Chemical Name | 1 |
| AUN | Autonomname | 1 |
| MF | Molecular Formula | 1 |
| FW | Formular Weight | 1 |
| LN | Lawson Number | 1 |
| CTYPE | Compound Type | 1 |
| CONSID | Constitution ID | 1 |
| TAUTID | Tautomer ID | 1 |
| BSO | Beilstein Citation | 1 |
| DED | Entry Date | 1 |
| DUPD | Update Date | 1 |

This substance also occurs in Reaction Documents:

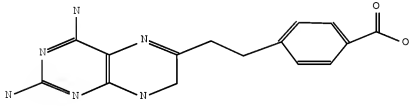
| Code | Name | Occurrence |
|---|---|---|
| RX | Reaction Documents | 2 |
| RXREA | Substance is Reaction Reactant | 1 |
| RXPRO | Substance is Reaction Product | 1 |

All References:
ALLREF

1. Nair, M. G., J.Org.Chem., CODEN: JOCEAH, 50(11), <1985>, 1879-1884; BABS-5699345

L61 ANSWER 8 OF 20 BEILSTEIN COPYRIGHT 2007 BEILSTEIN MDL on STN

| | |
|---|---|
| Beilstein Records (BRN): | 5613739 |
| Beilstein Pref. RN (BPR): | 96056-44-9 |
| CAS Reg. No. (RN): | 96056-44-9 |
| Chemical Name (CN): | 4-<2-(2,4-diamino-7,8-dihydro-pteridin-6-yl)-ethyl>-benzoic acid |
| Autonom Name (AUN): | 4-<2-(2,4-diamino-7,8-dihydro-pteridin-6-yl)-ethyl>-benzoic acid |
| Molec. Formula (MF): | C15 H16 N6 O2 |
| Molecular Weight (MW): | 312.33 |
| Lawson Number (LN): | 30747 |
| Compound Type (CTYPE): | heterocyclic |
| Constitution ID (CONSID): | 4965883 |
| Tautomer ID (TAUTID): | 5396728 |
| Beilstein Citation (BSO): | 6-26 |
| Entry Date (DED): | 1993/02/12 |
| Update Date (DUPD): | 1994/02/18 |



Field Availability:

| Code | Name | Occurrence |
|---|---|---|
| BRN | Beilstein Records | 1 |
| BPR | Beilstein Preferred RN | 1 |
| RN | CAS Registry Number | 1 |
| CN | Chemical Name | 1 |
| AUN | Autonomname | 1 |
| MF | Molecular Formula | 1 |
| FW | Formular Weight | 1 |
| LN | Lawson Number | 1 |
| CTYPE | Compound Type | 1 |
| CONSID | Constitution ID | 1 |
| TAUTID | Tautomer ID | 1 |
| BSO | Beilstein Citation | 1 |
| DED | Entry Date | 1 |
| DUPD | Update Date | 1 |

This substance also occurs in Reaction Documents:

| Code | Name | Occurrence |
|---|---|---|
| RX | Reaction Documents | 2 |

```
RXREA     Substance is Reaction Reactant              1
RXPRO     Substance is Reaction Product               1

All References:
ALLREF

 1. Nair, M. G., J.Org.Chem., CODEN: JOCEAH, 50(11), <1985>, 1879-1884;
    BABS-5699345
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L61 ANSWER 9 OF 20 BEILSTEIN COPYRIGHT 2007 BEILSTEIN MDL on STN

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Beilstein Records (BRN):          1117249
Beilstein Pref. RN (BPR):         50691-64-0
CAS Reg. No. (RN):                50691-64-0
Chemical Name (CN):               6-propyl-7,8-dihydro-pteridine-2,4-diamine
Autonom Name (AUN):               6-propyl-7,8-dihydro-pteridine-2,4-diamine
Molec. Formula (MF):              C9 H14 N6
Molecular Weight (MW):            206.25
Lawson Number (LN):               30710
Compound Type (CTYPE):            heterocyclic
Constitution ID (CONSID):         1074666
Tautomer ID (TAUTID):             1122047
Beilstein Citation (BSO):         5-26-17-00374
Entry Date (DED):                 1988/11/29
Update Date (DUPD):               1995/11/15
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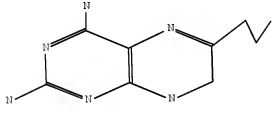


Field Availability:

| Code | Name | Occurrence |
|---|---|---|
| BRN | Beilstein Records | 1 |
| BPR | Beilstein Preferred RN | 1 |
| RN | CAS Registry Number | 1 |
| CN | Chemical Name | 1 |
| AUN | Autonomname | 1 |
| MF | Molecular Formula | 1 |
| FW | Formular Weight | 1 |
| LN | Lawson Number | 1 |
| CTYPE | Compound Type | 1 |
| CONSID | Constitution ID | 1 |
| TAUTID | Tautomer ID | 1 |
| BSO | Beilstein Citation | 1 |
| DED | Entry Date | 1 |
| DUPD | Update Date | 1 |

| | | |
|---|---|---|
| CDER | Chemical Derivative | 1 |
| MP | Melting Point | 1 |
| NMR | Nuclear Magnetic Resonance | 1 |

This substance also occurs in Reaction Documents:

| Code | Name | Occurrence |
|---|---|---|
| RX | Reaction Documents | 1 |
| RXPRO | Substance is Reaction Product | 1 |

All References:
ALLREF

1. Taylor et al., J.Amer.Chem.Soc., CODEN: JACSAT, 95, <1973>, 6413,6414,6416

L61 ANSWER 10 OF 20 MARPAT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 147:197412 MARPAT Full-text
TITLE: Use of hyaluronic acid as a carrier molecule for different classes of therapeutic active agents
INVENTOR(S): Norbedo, Stefano; Bosi, Susanna; Bergamin, Massimo; Khan, Riaz Ahmed; Murano, Erminio
PATENT ASSIGNEE(S): Eurand Pharmaceuticals Ltd., Ire.
SOURCE: PCT Int. Appl., 46pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2007085629 | A2 | 20070802 | WO 2007-EP50726 | 20070125 |
| WO 2007085629 | A3 | 20071129 | | |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

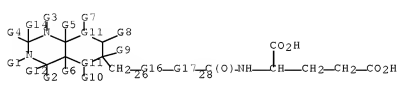
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA

PRIORITY APPLN. INFO.: IE 2006-49 20060125

AB The present invention refers to a drug delivery system consisting of hyaluronic acid and a therapeutic active agent, e.g., an analgesic, an antibiotic, an anesthetic, an antitumor agent, a CNS agent, a hormone, an immune agent, etc., whereby the active agent is covalently linked at the C-6 position of the N-acetyl-D-glucosamine residue of the hyaluronic acid with some exeptions. Pharmaceutical comps. obtained are in injectable form. Thus, 400 mg of 6-O-methanesulfonylhyaluronic acid TBA salt (obtained by treatment of hyaluronan TBA salt with methanesulfonyl chloride) and 333 mg of ibuprofen were dissolved in DMSO, cesium carbonate was added and the

suspension was heated to 70° for 20 h to afford 0.15 g of hyaluronic acid-ibuprofen.

MSTR 1



G11 = N
G12 = NH2
G14 = NH2
G16 = CH2
Patent location: claim 19

L61 ANSWER 11 OF 20 MARPAT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 146:288486 MARPAT Full-text
TITLE: Cleavage of antifolate compounds
INVENTOR(S): Melton, Roger; Atkinson, Anthony
PATENT ASSIGNEE(S): Protherics Medicines Development Limited, UK
SOURCE: PCT Int. Appl., 70pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2007023243 | A2 | 20070301 | WO 2005-GB3297 | 20050824 |
| WO 2007023243 | A3 | 20070907 | | |

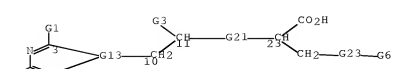
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA

PRIORITY APPLN. INFO.: WO 2005-GB3297 20050824

AB The present invention relates to the use of an enzyme having carboxypeptidase G activity, and in particular to its use in combating toxicity caused by Pemetrexed and related antifolate compds. The kinetic properties of carboxypeptidase G (glucarpidase) (Voraxaze) in cleavage of antifolates was determined and it was shown to decrease the plasma level of Pemetrexed to non-toxic levels in a human patient.

MSTR 1



G1 = NH2
G2 = NH2
G13 = 45-3 44-6 47-10

Patent location: claim 1
Note: or pharmaceutically acceptable salts and/or solvates
Note: substitution is restricted

L61 ANSWER 12 OF 20 MARPAT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 146:251859 MARPAT Full-text
TITLE: Preparation of condensed pyrimidine derivatives as inhibitors of folic acid-dependent enzymes.
INVENTOR(S): Stoicescu, Dan
PATENT ASSIGNEE(S): Cyprus
SOURCE: Eur. Pat. Appl., 27pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| EP 1754484 | A1 | 20070221 | EP 2005-107582 | 20050817 |
| R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, MK, YU | | | | |
| AU 2006281359 | A1 | 20070222 | AU 2006-281359 | 20060816 |
| CA 2583437 | A1 | 20070222 | CA 2006-2583437 | 20060816 |
| WO 2007020277 | A2 | 20070222 | WO 2006-EP65380 | 20060816 |
| WO 2007020277 | A3 | 20070426 | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, | | | | |

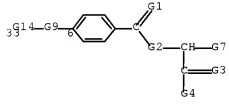
UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA

EP 1809292 A2 20070725 EP 2006-792859 20060816
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, MK, YU

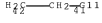
US 2007265444 A1 20071115 US 2007-663567 20070629
PRIORITY APPLN. INFO.: EP 2005-107582 20050817
WO 2006-EP65380 20060816

AB Title compds. [I; Z = O, S; B = NR2, CH2NR2, CH2CH2NR2, CH2CHR7, CH2O; R1 = NH2, OH; R2 = H, alkyl, alkenyl, alkynyl; R3 = CO2R8, COSR8, CONHR8, C(NH)SR8, etc.; R4 = H, CH2R5, CH2CH2R5; R7 = H, alkyl, alkoxy; R8 = H, Me, Et, Pr, Me2CH, Bu, Me3C, Me2CHCH2; A = Q1, Q2; X, Y = atoms to form (substituted) (aromatic) (hetero)cyclyl], were prepared Thus, title compound (II) (preparation from 3-chloropropanoyl chloride, Et cyanoacetate, α-bromo-p-nitroacetophenone, and 2,4-diamino-6-bromomethylpteridine given) inhibited dihydrofolate reductase with a relative IC50 = 0.75, vs 1.0 for methotrexate.

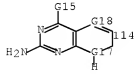
MSTR 1




G9 = 42-33 41-6




G14 = 114




G15 = NH2
G17 = N
G18 = N
Patent location: claim 1

Note: substitution is restricted
Note: or pharmaceutically acceptable salts

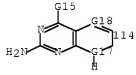
NSTR 2

G14—G9

G9 = 332

3G20—G21

G14 = 114




G15 = NH2
G17 = N
G18 = N
G20 = (1-2) CH2
Patent location: claim 22

REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L61 ANSWER 13 OF 20 MARPAT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 146:725 MARPAT Full-text
TITLE: Antiproliferative hyaluronic acid conjugates and preparation thereof
INVENTOR(S): Murano, Erminio; Flaibani, Antonella; Bergamin, Massimo; Norbedo, Stefano; Sorbi, Claudia; Khan, Riaz Ahmed
PATENT ASSIGNEE(S): Eurand Pharmaceuticals Limited, Ire.
SOURCE: PCT Int. Appl., 33pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2006122954 | A2 | 20061123 | WO 2006-EP62388 | 20060517 |
| WO 2006122954 | A3 | 20070315 | | |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,

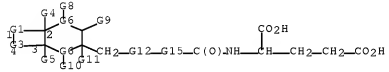
CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: IE 2005-328 20050518

AB The invention discloses esterified conjugates of hyaluronic acid having antiproliferative activity. Preparation of hyaluronic acid conjugates with methotrexate are described.

MSTP 1




G1 = 11-4 12-2


G2 = NH2
G3 = 19-3 20-1


G6 = N
G12 = 43




Patent location: claim 1

L61 ANSWER 14 OF 20 MARPAT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 145:46083 MARPAT Full-text
TITLE: Processes for preparation of aminotetrahydropteridines
INVENTOR(S): Noe, Christian
PATENT ASSIGNEE(S): Vasopharm Biotech G.m.b.H., Germany
SOURCE: PCT Int. Appl., 38 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2006058669 | A2 | 20060608 | WO 2005-EP12644 | 20051125 |
| WO 2006058669 | A3 | 20060817 | | |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

| | | | | |
|---|---|---|---|---|
| EP 1669355 | A1 | 20060614 | EP 2004-28614 | 20041202 |

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, BA, HR, IS, YU

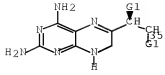
PRIORITY APPLN. INFO.: EP 2004-28614 20041202
OTHER SOURCE(S): CASREACT 145:46083

AB The present invention provides a process for preparing aminotetrahydropteridines I [wherein A and B = independently H or hydroxy protective groups; Z = H or dithioacetal moiety] comprising transformation of D-ribose into open chain osone with protected hydroxy groups, followed by reaction with tetraaminopyrimidine, reduction, and cleavage of the protective groups. For example, D-ribose was transformed to 3,4-O-benzyl-5-desoxy-L-erythro-pentos-2-ulose in a multi-step synthesis. The osone obtained in previous step was treated with hydroxylamine, followed by reaction with tetraaminopyrimidine dihydrochloride and hydrogenation to give II. The title compds. are useful as inhibitors of NO-synthase.

MSTR 1A

G3—G11

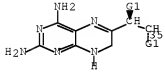
G3 = 35



Patent location: claim 1
Note: also incorporates claim 2, 3 and 4

MGTR 1B

G3 = 35



Patent location: claim 1
Note: also incorporates claim 2, 3 and 4

L61 ANSWER 15 OF 20 MARPAT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 143:299139 MARPAT Full-text
TITLE: Use of enzyme carboxypeptidase G for combating toxicity caused by an antifolate compound
INVENTOR(S): Melton, Roger; Atkinson, Anthony
PATENT ASSIGNEE(S): Protherics Molecular Design Limited, UK
SOURCE: PCT Int. Appl., 54 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2005084695 | A2 | 20050915 | WO 2005-GB751 | 20050228 |
| WO 2005084695 | A3 | 20051208 | | |

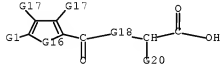
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

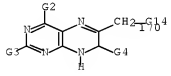
| | | | | | |
|---|---|---|---|---|---|
| AU | 2005218987 | A1 | 20050915 | AU 2005-218987 | 20050228 |
| CA | 2557610 | A1 | 20050915 | CA 2005-2557610 | 20050228 |
| EP | 1727548 | A2 | 20061206 | EP 2005-717830 | 20050228 |
| | R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR | | | | |
| CN | 1950088 | A | 20070418 | CN 2005-80013842 | 20050228 |
| BR | 2005008053 | A | 20070717 | BR 2005-8053 | 20050228 |
| JP | 2007524711 | T | 20070830 | JP 2007-500299 | 20050228 |
| KR | 2007036023 | A | 20070402 | KR 2006-717341 | 20060828 |
| IN | 2006DN04935 | A | 20070817 | IN 2006-DN4935 | 20060828 |
| US | 2007243182 | A1 | 20071018 | US 2007-590789 | 20070212 |
| PRIORITY APPLN. INFO.: | | | | GB 2004-4487 | 20040228 |
| | | | | WO 2005-GB751 | 20050228 |

AB A method of combating toxicity caused by an antifolate compound in an individual who has been administered the compound The method comprises administering an enzyme that has activity to the individual. A method of cleaving a compound comprising a structural fragment of Formula I (A6 represents O or S; R8 represents H or one or two substituents selected from halo, C1-4 alkyl and C1-4 alkoxy; R3 represents H or C1-4 alkyl; R4 represents -CH2C(R9a)(R9b)-D where R9a and R9b independently represent H or C1-4 alkyl, or R9a and R9b together represent =C(H)R10 and R10 represents H or C-4-alkyl and D represents C(O)OH, tetrazol-5-yl, etc.), the method comprising contacting the compound comprising the structural fragment of Formula I with an enzyme that has carboxypeptidase G activity.

MSTR 1




G1 = 170




G2 = NH2
G3 = NH2
G14 = 95

US-G15

Patent location: claim 1
Note: or pharmaceutically acceptable salts or solvates

L61 ANSWER 16 OF 20 MARPAT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 143:153229 MARPAT Full-text
TITLE: Preparation of pharmaceutical compositions containing 4-amino-7,8-dihydropteridines and their use for the treatment of diseases which are caused by an increased nitric oxide level
INVENTOR(S): Doblhofer, Robert; Tegtmeier, Frank
PATENT ASSIGNEE(S): Vasopharm Biotech G.m.b.H., Germany
SOURCE: PCT Int. Appl., 46 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

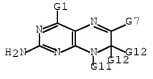
| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2005063752 | A1 | 20050714 | WO 2003-EP14970 | 20031230 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| CA 2552195 | A1 | 20050714 | CA 2003-2552195 | 20031230 |
| AU 2003290127 | A1 | 20050721 | AU 2003-290127 | 20031230 |
| EP 1699793 | A1 | 20060913 | EP 2003-782489 | 20031230 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, SK | | | | |
| JP 2007525407 | T | 20070906 | JP 2005-512684 | 20031230 |
| IN 2006DN03444 | A | 20070831 | IN 2006-DN3444 | 20060615 |

PRIORITY APPLN. INFO.: WO 2003-EP14970 20031230

AB The present invention relates to the area of NO synthase inhibition and, more particularly, relates to novel 4-amino-7,8-dihydropteridines, e.g., I [R1, R2 = H, C1-20-alkyl, C1-20-alkenyl, C1-20-alkynyl, C3-8-cycloalkyl, cycloalkenyl, (cycloalkyl)alkyl, aryl, (c1-3-alkyl)aryl, etc.; NR1R2 = 3- to 8-membered ring (optionally containing 1 or 2 other heteroatoms - O, S, N); R4 = C1-20-alkyl, C1-20-alkenyl, C1-20-alkynyl, C3-8-cycloalkyl, cycloalkenyl, (cycloalkyl)alkyl, aryl, (C1-3-alkyl)aryl, etc.; R6, R7 = F, Cl, I, Br, O-(C1-10-alkyl), OPh, OC(:O)(C1-10-alkyl), OC(:O)aryl, NR8R9, oxo, Ph, C(:O)(C1-5-alkyl), CF3, CN, CONR8R9, CO2H, C(:O)O-(C1-5-alkyl), C(:O)O-aryl, S(O)n-(C1-5-alkyl), SO2NR8R9; R8 = H, C1-20-alkyl; R9 = H, C1-20-alkyl, aryl (preferably Ph); R11 = H, C1-20-alkyl, aryl, CO-alkyl, CO-aryl; R12, R13 = H, C1-10-alkyl, aryl, O-(C1-10-alkyl), OPh, OC(:O)-C1-10-alkyl, OC(:O)-aryl, NR8R9, Ph, C(:O)-C1-10-alkyl, CF3, CN, CONR8R9, CO2H, etc.; aryl = (un)substituted Ph, naphthyl, heteroaryl; heteroaryl = 5- to 7-membered ring (optionally containing an addnl. heteroatom - O, N, S); n = 0 - 2], or their

pharmaceutically acceptable acid addition salts, hydrates and esters, pharmaceutical compns. containing said compds., and the use of said compds. in the treatment of a disorder characterized by a disturbed nitric oxide level. The patent particularly excludes compds. II [R21, R22, R23, R24 = ; R25 = H, Me, CH2OH, CHO, (un)branched C1-9-alkyl, (CHOH)nY, (CHOH)n(CH2)mW; Y = H, C1-9-alkyl; W = H, OH; n, m = 1 - 20]. Thus, 4-[(Cyclohexylmethyl)amino]-5,6,7,8-tetrahydrobiopterin (III) was prepared from biopterin (IV) via acetylation with Ac2O in pyridine, reaction with PhCH2CH2OH in dioxane containing Ph3P, amination with (cyclohexylmethyl)amine in dioxane, and hydrogenation in CF2CO4H containing catalytic PtO2. The in vivo stability [t1/2 = << 5 min. (tetrahydro); t1/2 = 48 min. (dihydro)] and NO release inhibitor activity for I was determined

MSTR 1




G1 = NH2
G7 = alkyl <containing 1-20 C>
(opt. substd. by 1 or more G17)
Patent location: claim 1
Note: substitution is restricted
Note: and tautomeric forms and mixtures and physiologically tolerated salts, hydrates and esters
Note: additional oxo formation also claimed
Stereochemistry: and stereoisomeric forms and mixtures

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L61 ANSWER 17 OF 20 MARPAT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 142:404279 MARPAT Full-text
TITLE: Use of pteridine derivatives for the treatment of increased intracranial pressure and secondary ischemia
INVENTOR(S): Doblhofer, Robert; Tegtmeier, Frank
PATENT ASSIGNEE(S): Vasopharm Biotech GmbH, Germany
SOURCE: PCT Int. Appl., 41 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2005037286 | A1 | 20050428 | WO 2003-EP3096 | 20030325 |
| W: US | | | | |
| CA 2519919 | A1 | 20041007 | CA 2003-2519919 | 20031008 |
| WO 2004084906 | A1 | 20041007 | WO 2003-EP11138 | 20031008 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, | | | | |

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GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK,
LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ,
OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM,
TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,
BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

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| AU | 2003293607 | A1 | 20041018 | AU 2003-293607 | 20031008 |
| EP | 1605947 | A1 | 20051221 | EP 2003-788945 | 20031008 |
| EP | 1605947 | B1 | 20060802 | | |

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK

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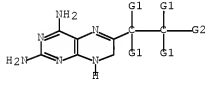
| CN | 1758913 | A | 20060412 | CN 2003-80110211 | 20031008 |
| JP | 2006514965 | T | 20060518 | JP 2004-569858 | 20031008 |
| AT | 334681 | T | 20060815 | AT 2003-788945 | 20031008 |
| ES | 2270151 | T3 | 20070401 | ES 2003-3788945 | 20031008 |
| MX | 2005PA09491 | A | 20060222 | MX 2005-PA9491 | 20050906 |
| US | 2007032498 | A1 | 20070208 | US 2006-549200 | 20060703 |
| PRIORITY APPLN. INFO.: | | | | WO 2003-EP3096 | 20030325 |
| | | | | WO 2003-EP11138 | 20031008 |

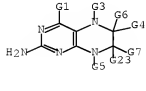
AB The invention discloses the use of pteridine derivs. for treating increased intracranial pressure and/or secondary ischemia. Compound preparation is included.

MSTP 2




Patent location: claim 4

MSTR 3




G1 = NH2
G4 = alkynyl (opt. substd.)
Patent location: claim 6
Note: and physiologically tolerated salts, hydrates, and

esters, and tautomers
Stereochemistry: and stereoisomers

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L61 ANSWER 18 OF 20 MARPAT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 141:307610 MARPAT Full-text
TITLE: Use of pteridine derivatives for the treatment of increased intracranial pressure, secondary ischemia, and disorders associated with an increased level of cytotoxic reactive oxygen species
INVENTOR(S): Doblhofer, Robert; Tegtmeier, Frank
PATENT ASSIGNEE(S): Vasopharm Biotech G.m.b.H., Germany
SOURCE: PCT Int. Appl., 47 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2004084906 | A1 | 20041007 | WO 2003-EP11138 | 20031008 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
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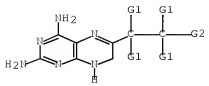
| WO 2005037286 | A1 | 20050428 | WO 2003-EP3096 | 20030325 |
| W: US | | | | |
| CA 2519919 | A1 | 20041007 | CA 2003-2519919 | 20031008 |
| AU 2003293607 | A1 | 20041018 | AU 2003-293607 | 20031008 |
| EP 1605947 | A1 | 20051221 | EP 2003-788945 | 20031008 |
| EP 1605947 | B1 | 20060802 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK | | | | |
| JP 2006514965 | T | 20060518 | JP 2004-569858 | 20031008 |
| MX 2005PA09491 | A | 20060222 | MX 2005-PA9491 | 20050906 |
| US 2007032498 | A1 | 20070208 | US 2006-549200 | 20060703 |
| PRIORITY APPLN. INFO.: | | | WO 2003-EP3096 | 20030325 |
| | | | WO 2003-EP11138 | 20031008 |

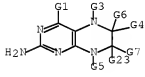
AB The present invention relates to the use of pteridine derivs. for the treatment of increased intracranial pressure, secondary ischemia, and disorders associated with an increased level of cytotoxic reactive oxygen species. H4-aminobiopterin (preparation given) caused a clear concentration dependent contraction of both rat basilar arteries and middle cerebral arteries.

MSTP 2



Patent location: claim 4

MSTR 3



G1 = NH2
G4 = alkynyl (opt. substd.)
Patent location: claim 6
Note: and physiologically tolerated salts, hydrates, and esters, and tautomers
Stereochemistry: and stereoisomers

REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L61 ANSWER 19 OF 20 MARPAT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 135:258794 MARPAT Full-text
TITLE: Polysaccharide esters of N-derivatives of glutamic acid, their preparation and use
INVENTOR(S): Miglierini, Giuliana; Stucchi, Luca; Rastrelli, Alessandro
PATENT ASSIGNEE(S): Societa Cooperativa Centro Ricerche Poly-Tech A Responsabilita Limitata, Italy
SOURCE: PCT Int. Appl., 28 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2001068105 | A1 | 20010920 | WO 2001-EP3050 | 20010316 |

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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

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| IT | 2000MI0559 | A1 | 20010917 | IT 2000-MI559 | 20000317 |
| IT | 1318403 | B1 | 20030825 | | |
| CA | 2403063 | A1 | 20010920 | CA 2001-2403063 | 20010316 |
| BR | 2001009294 | A | 20021217 | BR 2001-9294 | 20010316 |
| EP | 1274446 | A1 | 20030115 | EP 2001-931536 | 20010316 |
| EP | 1274446 | B1 | 20050914 | | |

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

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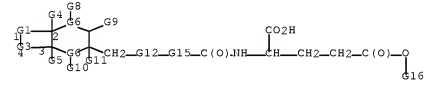
|---|---|---|---|---|---|
| JP | 2003526720 | T | 20030909 | JP 2001-566669 | 20010316 |
| AT | 304363 | T | 20050915 | AT 2001-931536 | 20010316 |
| ES | 2248322 | T3 | 20060316 | ES 2001-1931536 | 20010316 |
| AU | 784655 | B2 | 20060518 | AU 2001-58286 | 20010316 |
| MX | 2002PA09057 | A | 20040906 | MX 2002-PA9057 | 20020917 |
| ZA | 2002008299 | A | 20031215 | ZA 2002-8299 | 20021015 |
| US | 2003158125 | A1 | 20030821 | US 2003-221703 | 20030127 |
| US | 6844328 | B2 | 20050118 | | |
| US | 2005065112 | A1 | 20050324 | US 2004-950879 | 20040927 |

PRIORITY APPLN. INFO.:

IT 2000-MI559 20000317
WO 2001-EP3050 20010316
US 2003-221703 20030127

AB These polysaccharidic esters have antiproliferative activity and are characterized by a low systemic toxicity. The esters are used in the prevention and therapy of diseases caused by cellular hyperproliferation, particularly psoriasis, tumors, rheumatoid arthritis, or intestinal inflammatory pathologies. I (R2,R4 = NH2; X,Y = N; Z = NMe; Ar = 1,4-phenylene) was esterified with halogenated scleroglucan.

MSTR 1




G1 = 11-4 12-2


G2 = NH2
G3 = 19-3 20-1


G6 = N
G12 = 43


Patent location: claim 1

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L61 ANSWER 20 OF 20 MARPAT COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 134:237499 MARPAT Full-text
TITLE: Preparation of N-substituted-4-aminopteridines as NO synthase inhibitors for use as pharmaceuticals
INVENTOR(S): Pfleiderer, Wolfgang; Schmidt, Harald; Froehlich, Lothar; Kotsonis, Peter; Taghavi-Moghadam, Shahriyar
PATENT ASSIGNEE(S): Vasopharm Biotech G.m.b.H. & Co. K.-G., Germany
SOURCE: PCT Int. Appl., 43 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2001021619 | A1 | 20010329 | WO 2000-EP8833 | 20000911 |
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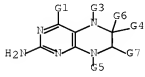
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| DE 19944767 | A1 | 20010329 | DE 1999-19944767 | 19990917 |
| EP 1216246 | A1 | 20020626 | EP 2000-964154 | 20000911 |
| EP 1216246 | B1 | 20050824 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL | | | | |
| JP 2004522690 | T | 20040729 | JP 2001-524995 | 20000911 |
| AT 302778 | T | 20050915 | AT 2000-964154 | 20000911 |
| ES 2248124 | T3 | 20060316 | ES 2000-964154 | 20000911 |
| US 6844343 | B1 | 20050118 | US 2002-70976 | 20020719 |
| PRIORITY APPLN. INFO.: | | | DE 1999-19944767 | 19990917 |
| | | | WO 2000-EP8833 | 20000911 |

AB Pteridines, such as I [R1, R2 = H, alkyl, aryl, arylalkyl; R1R2 = nitrogen bound heterocyclyl, such as 1-piperidinyl or 4-morpholinyl; R4 = alkyl, alkenyl, alkynyl, cycloalkenyl, aryl, etc.; R3, R5 = acyl, aroyl, R6 = R7 = H,

or R3R6 = R5R7 = bond;], were prepared for pharmaceutical use. Thus, pteridine II was prepared via cyclocondensation of N4,N4-dimethylpyrimidinetetramine dihydrochloride and phenylglyoxal monoxime. The prepared pteridines were tested for nitric oxide synthase inhibiting activity.

MSTP 1




G1 = 20


G4 = alkyl (opt. substd. by 1 or more G8)
Patent location: claim 1
Note: and physiologically useful salts, hydrates, and esters
Stereochemistry: and stereoisomers and tautomers

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

# Structure Search
# First 10, Middle 10 and Last 10 Results

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USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
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COPYRIGHT (C) 2007 AMERICAN CHEMICAL SOCIETY (ACS)
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FILE COVERS 1907 - 27 Dec 2007  VOL 147 ISS 26
FILE LAST UPDATED: 26 Dec 2007  (20071226/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

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'OBI' IS DEFAULT SEARCH FIELD FOR 'HCAPLUS' FILE

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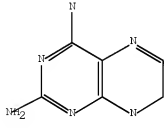


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* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY -  AVAILABLE VIA OFFLINE PRINT *

Structure attributes must be viewed using STN Express query preparation.
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HITSTR L62 205-215

L62  ANSWER 1 OF 215  HCAPLUS  COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER:         2007:633002  HCAPLUS  Full-text
DOCUMENT NUMBER:          147:73054
TITLE:                    Synthesis of methotrexate-containing heterodimeric
                          molecules
INVENTOR(S):              Murthi, Krishna K.; Smith, Chase C.
PATENT ASSIGNEE(S):       Gpc Biotech, Inc., USA
SOURCE:                   U.S., 54pp.
                          CODEN: USXXAM
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.           KIND   DATE        APPLICATION NO.          DATE
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     US 7230101            B1    20070612    US 2003-651340           20030828 <--
PRIORITY APPLN. INFO.:                       US 2002-407131P     P    20020828 <--
OTHER SOURCE(S):          MARPAT 147:73054
ED   Entered STN:  13 Jun 2007
GI
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* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The present invention relates to novel compns. of methotrexate-containing heterodimeric probe mols., also known as chemical inducers of dimerization (CID), useful in three-hybrid assays. The invention further relates to synthesis of said compns. and their intermediates. Another aspect of the invention is a method for using the heterodimeric probe mols. described herein in drug screens to identify potential protein targets to a given ligand, optimize protein-ligand interactions, or identify potential ligands for a given protein target (no data). Thus, methotrexate derivative (I) was condensed with purvalanol B derivative (II; R = H) using 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride, HOBt, and diisopropylethylamine in CH2C12 followed by treatment with 90% aqueous CF3CO2H solution to give II (R = Q) as a methotrexate-containing heterodimeric probe which is a ligand of both DNA binding fusion protein and activation domain fusion protein.

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IT   73978-41-3, 2,4-Diaminopyrimido[4,5-b]pyrazine-6-methanol
     monohydrochloride
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (preparation of methotrexate-containing heterodimeric probe mols. as
chemical
        inducers of dimerization in three-hybrid assays or in drug screens to
        identify potential protein targets)
RN   73978-41-3  HCAPLUS
CN   6-Pteridinemethanol, 2,4-diamino-, hydrochloride (1:1)  (CA INDEX NAME)
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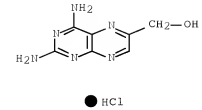

L62 ANSWER 2 OF 215 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:1335074 HCAPLUS Full-text
DOCUMENT NUMBER: 144:69859
TITLE: Indoles, pteridines, pyridopyrazines, and benzotriazines as vasculostatic agents, their preparation, pharmaceutical compositions and use in therapy
INVENTOR(S): Wrasidlo, Wolfgang; Doukas, John; Royston, Ivor; Noronha, Glenn; Hood, John D.; Dneprovskaia, Elena; Gong, Xianchang; Splittgerber, Ute; Zhao, Ningning
PATENT ASSIGNEE(S): Targegen, Inc., USA
SOURCE: U.S. Pat. Appl. Publ., 95 pp., Cont.-in-part of U.S. Ser. No. 679,209.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | | DATE | |
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| US 2005282814 | A1 | 20051222 | US 2005-105845 | | 20050413 | <-- |
| US 2004167198 | A1 | 20040826 | US 2003-679209 | | 20031002 | <-- |
| US 7208493 | B2 | 20070424 | | | | |
| US 2007208019 | A1 | 20070906 | US 2007-653190 | | 20070111 | <-- |
| PRIORITY APPLN. INFO.: | | | US 2002-415981P | P | 20021003 | <-- |
| | | | US 2003-440234P | P | 20030114 | <-- |
| | | | US 2003-443752P | P | 20030129 | <-- |
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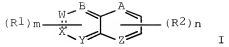
| | | | US 2003-479295P | P | 20030617 | <-- |
| | | | US 2003-679209 | A2 | 20031002 | <-- |

OTHER SOURCE(S): CASREACT 144:69859; MARPAT 144:69859
ED Entered STN: 23 Dec 2005
GI



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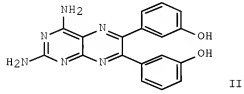


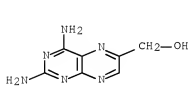
II

AB The invention relates to nitrogen heterocyclic compds. of formula I, which are useful for treating disorders associated with compromised vasculostasis. In compds. I, each of A, B, W, X, Y, and Z is independently selected from C, C(O), N, and NR3, where R3 is H or (un)substituted alkyl; each R1 is independently halo, OR4, N(R4)2, or SR4, where R4 is H, lower alkyl, aryl, heteroaryl, etc.; each R2 is independently halo, OR5, N(R5)2, SR5, OPO3H2, (un)substituted alkyl, (un)substituted aryl, (un)substituted heteroaryl, where R5 is H, lower alkyl, aryl, heteroaryl, etc.; and each of m and n is independently an integer from 1 to 4. The invention also relates to the preparation of I, pharmaceutical compns. comprising a compound I and a pharmaceutically acceptable carrier, as well as to the use of the compns. for the treatment of a variety of disorders including stroke, myocardial infarction, cancer, ischemia/reperfusion injury, autoimmune diseases such as rheumatoid arthritis, eye diseases such as retinopathies or macular degeneration, inflammatory diseases, vascular leakage syndrome, edema, transplant rejection, adult/acute respiratory distress syndrome (ARDS), and the like. Cyclocondensation of 3,3'-dihydroxybenzil with 2,4,5,6-tetraaminopyrimidine sulfate results in the formation of diaminopteridine II. Compound II expresses an IC50 value of 83 nM in an assay for the inhibition of the human p120γ subunit of PI3 kinase and results in 65% reduction of myocardial infarction in rats.

IT 76145-91-0, (2,4-DiaminoPteridin-6-yl)-methanol hydrobromide
RL: RCT (Reactant); RACT (Reactant or reagent)
(starting material; preparation of vasculostatic agents and use for treatment of disorders associated with compromised vasculostasis)

RN 76145-91-0 HCAPLUS

CN 6-Pteridinemethanol, 2,4-diamino-, hydrobromide (9CI) (CA INDEX NAME)

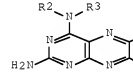


● x HBr

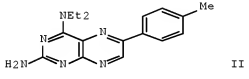
L62 ANSWER 3 OF 215 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:561514 HCAPLUS Full-text
DOCUMENT NUMBER: 143:211928
TITLE: Preparation of Pteridine derivatives as nitric oxide synthase inhibitors
INVENTOR(S): Yao, Qizheng
PATENT ASSIGNEE(S): China Pharmaceutical University, Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing Gongkai Shuomingshu, No pp. given
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| CN 1546491 | A | 20041117 | CN 2003-10106588 | 20031210 <-- |
| PRIORITY APPLN. INFO.: | | | CN 2003-10106588 | 20031210 <-- |

OTHER SOURCE(S): CASREACT 143:211928; MARPAT 143:211928
ED Entered STN: 29 Jun 2005
GI



I

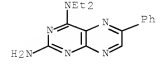


II

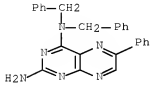
AB The title compds. I [wherein R = H, (un)substituted alkyl, alkoxy, etc.; R1 = H, Ph, alkyl, etc.; R2 and R3 = independently alkyl, PhCH2, etc.] or pharmaceutically acceptable salts thereof are prepared as NO synthetase inhibitors for the prevention and treatment of diseases caused by NO level rise. For example, the compound II was prepared II inhibited NO generation with ID50 of 14.85 μM.

IT 247913-54-8P 247913-56-0P 862503-57-9P
862503-60-4P 862503-61-5P 862503-62-6P
862503-64-8P 862503-65-9P 862503-66-0P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of pteridine derivs. as nitric oxide synthase inhibitors)

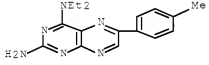
RN 247913-54-8 HCAPLUS
CN 2,4-Pteridinediamine, N4,N4-diethyl-6-phenyl- (CA INDEX NAME)



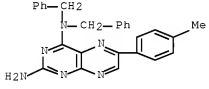
RN 247913-56-0 HCAPLUS
CN 2,4-Pteridinediamine, 6-phenyl-N4,N4-bis(phenylmethyl)- (CA INDEX NAME)



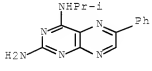
RN 862503-57-9 HCAPLUS
CN 2,4-Pteridinediamine, N4,N4-diethyl-6-(4-methylphenyl)- (CA INDEX NAME)



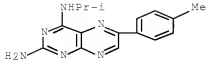
RN 862503-60-4 HCAPLUS
CN 2,4-Pteridinediamine, 6-(4-methylphenyl)-N4,N4-bis(phenylmethyl)- (CA INDEX NAME)



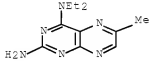
RN 862503-61-5 HCAPLUS
CN 2,4-Pteridinediamine, N4-(1-methylethyl)-6-phenyl- (CA INDEX NAME)



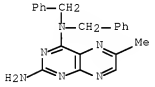
RN 862503-62-6 HCAPLUS
CN 2,4-Pteridinediamine, N4-(1-methylethyl)-6-(4-methylphenyl)- (CA INDEX NAME)



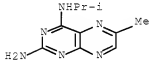
RN 862503-64-8 HCAPLUS
CN 2,4-Pteridinediamine, N4,N4-diethyl-6-methyl- (CA INDEX NAME)



RN 862503-65-9 HCAPLUS
CN 2,4-Pteridinediamine, 6-methyl-N4,N4-bis(phenylmethyl)- (CA INDEX NAME)



RN 862503-66-0 HCAPLUS
CN 2,4-Pteridinediamine, 6-methyl-N4-(1-methylethyl)- (CA INDEX NAME)

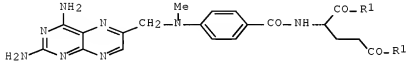


L62 ANSWER 4 OF 215 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:371673 HCAPLUS Full-text
DOCUMENT NUMBER: 142:392421
TITLE: Preparation of methotrexate
INVENTOR(S): Amonkar, Ashok Jaganath; Ganu, Ulhas Kashinath; Indap, Manohar Atmaram
PATENT ASSIGNEE(S): Department of Atomic Energy, Government of India, India
SOURCE: Indian, 29 pp.
CODEN: INXXAP
DOCUMENT TYPE: Patent

LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| IN 182947 | A1 | 19990814 | IN 1998-BO236 | 19980422 <-- |
| PRIORITY APPLN. INFO.: | | | IN 1998-BO236 | 19980422 <-- |

OTHER SOURCE(S): CASREACT 142:392421
ED Entered STN: 02 May 2005
GI

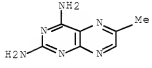


I

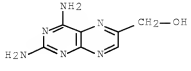
AB Preparation of methotrexate I [R = OH] via the N-alkylation of di-Et N-(p-N-methylaminobenzoyl)glutamate by 2,4-diamino-6- (bromomethyl)pteridine was disclosed. For example, a suspension of di-Et N-(p-N-methylaminobenzoyl)glutamate (6.7 mmol), 2,4-diamino-6- (bromomethyl)pteridine HBr (5.8 mmol) in di-Me N-acetamide was stirred at 55°C for 4 h, after work-up afforded the di-Et ester of methotrexate I [R = OH] in 66.5% yield. In P-388 lymphocytic leukemia mice survival assays, the sodium salt of compound I [R = ONa], at 2.5 mg/kg dosage over 1, 5, 9 days exhibited a medium survival rate of 19.5 days.

IT 708-74-7P 945-24-4P 57963-59-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of methotrexate)

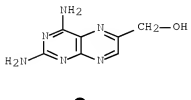
RN 708-74-7 HCAPLUS
CN 2,4-Pteridinediamine, 6-methyl- (CA INDEX NAME)



RN 945-24-4 HCAPLUS
CN 6-Pteridinemethanol, 2,4-diamino- (CA INDEX NAME)



RN 57963-59-4 HCAPLUS
CN 6-Pteridinemethanol, 2,4-diamino-, monohydrobromide (9CI) (CA INDEX NAME)



● HBr

L62 ANSWER 5 OF 215 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:259882 HCAPLUS Full-text
DOCUMENT NUMBER: 142:336393
TITLE: Preparation of pteridine derivatives for the treatment of septic shock and TNF-α-related diseases.
INVENTOR(S): Waer, Mark Jozef Albert; Herdewijn, Piet Andre Maurits Maria; De Jonghe, Steven Cesar Alfons; Marchand, Arnaud Didier Marie; Yuan, Lin; El Hassane, Sefrioui
PATENT ASSIGNEE(S): 4 Aza Bioscience Nv, Belg.
SOURCE: PCT Int. Appl., 79 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 8
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2005025574 | A2 | 20050324 | WO 2004-EP10198 | 20040913 <-- |
| WO 2005025574 | A3 | 20050630 | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| GB 2405793 | A | 20050316 | GB 2003-21384 | 20030912 <-- |
| GB 2413324 | A | 20051026 | GB 2004-8955 | 20040422 |
| AU 2004271721 | A1 | 20050324 | AU 2004-271721 | 20040913 <-- |
| CA 2534549 | A1 | 20050324 | CA 2004-2534549 | 20040913 <-- |
| EP 1663244 | A2 | 20060607 | EP 2004-765120 | 20040913 <-- |
| EP 1663244 | B1 | 20070815 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK | | | | |
| JP 2007533617 | T | 20071122 | JP 2006-525783 | 20040913 <-- |
| US 2007004721 | A1 | 20070104 | US 2006-595161 | 20060310 <-- |
| PRIORITY APPLN. INFO.: | | | GB 2003-21384 A | 20030912 <-- |

GB 2004-8955 A 20040422
WO 2004-EP10198 W 20040913

OTHER SOURCE(S): CASREACT 142:336393; MARPAT 142:336393
ED Entered STN: 25 Mar 2005
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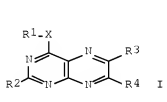


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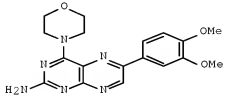
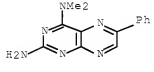



II

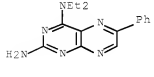
AB Pteridine derivs. of formula I [X = O, SOm; m = 0-2; R1 = alkyl, cycloalkyl, aryl, arylalkyl, heterocyclyl, etc.; R2 = amino, acylamino, carbamoyl, ureido, etc.; R3, R4 = H, halo, alkyl, carboxyalkyl, arylamino, etc.; R3R4 = alkylene, etc.] are prepared for the manufacture of a medicament for the prevention or treatment of septic shock and TNF-α related disorders. Thus, II was prepared, and had IC50 of 0.4 μM against TNF-α.

IT 247913-51-5P 247913-54-8P 247913-56-0P
278799-96-5P 278800-02-5P 278800-24-1P
278800-27-4P 278800-29-6P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of pteridine derivs. for treatment of septic shock and TNF-α-related diseases)

RN 247913-51-5 HCAPLUS
CN 2,4-Pteridinediamine, N4,N4-dimethyl-6-phenyl- (CA INDEX NAME)

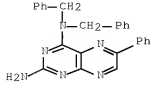



RN 247913-54-8 HCAPLUS
CN 2,4-Pteridinediamine, N4,N4-diethyl-6-phenyl- (CA INDEX NAME)

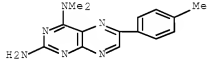



RN 247913-56-0 HCAPLUS

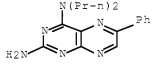
CN 2,4-Pteridinediamine, 6-phenyl-N4,N4-bis(phenylmethyl)- (CA INDEX NAME)



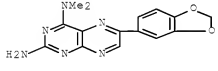
RN 278799-96-5 HCAPLUS
CN 2,4-Pteridinediamine, N4,N4-dimethyl-6-(4-methylphenyl)- (CA INDEX NAME)



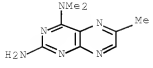
RN 278800-02-5 HCAPLUS
CN 2,4-Pteridinediamine, 6-phenyl-N4,N4-dipropyl- (CA INDEX NAME)



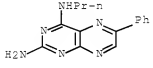
RN 278800-24-1 HCAPLUS
CN 2,4-Pteridinediamine, 6-(1,3-benzodioxol-5-yl)-N4,N4-dimethyl- (CA INDEX NAME)



RN 278800-27-4 HCAPLUS
CN 2,4-Pteridinediamine, N4,N4,6-trimethyl- (CA INDEX NAME)




RN 278800-29-6 HCAPLUS
CN 2,4-Pteridinediamine, 6-phenyl-N4-propyl- (CA INDEX NAME)




L62 ANSWER 6 OF 215 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:228920 HCAPLUS Full-text
DOCUMENT NUMBER: 142:297927
TITLE: Pteridine derivatives for treating TNF-alpha related disorders
INVENTOR(S): Herdewijn, Piet; Waer, Mark; De Jonghe, Steven Cesar Alfons; Yuan, Lin; El Hassane, Sefrioui
PATENT ASSIGNEE(S): 4 AZA Bioscience NV, Belg.
SOURCE: Brit. UK Pat. Appl., 72 pp.
CODEN: BAXXDU
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 8
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| GB 2405793 | A | 20050316 | GB 2003-21384 | 20030912 <-- |
| AU 2004271721 | A1 | 20050324 | AU 2004-271721 | 20040913 <-- |
| CA 2534549 | A1 | 20050324 | CA 2004-2534549 | 20040913 <-- |
| WO 2005025574 | A2 | 20050324 | WO 2004-EP10198 | 20040913 <-- |
| WO 2005025574 | A3 | 20050630 | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| EP 1663244 | A2 | 20060607 | EP 2004-765120 | 20040913 <-- |
| EP 1663244 | B1 | 20070815 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK | | | | |
| AT 369861 | T | 20070915 | AT 2004-765120 | 20040913 <-- |

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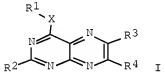
|---|---|---|---|---|---|---|
| JP 2007533617 | T | 20071122 | JP 2006-525783 | | 20040913 | <-- |
| US 2007004721 | A1 | 20070104 | US 2006-595161 | | 20060310 | <-- |
| PRIORITY APPLN. INFO.: | | | GB 2003-21384 | A | 20030912 | <-- |
| | | | GB 2004-8955 | A | 20040422 | |
| | | | WO 2004-EP10198 | W | 20040913 | |

OTHER SOURCE(S): MARPAT 142:297927
ED Entered STN: 16 Mar 2005
GI

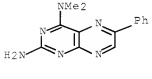


I

AB This invention relates to the use of a group of pteridine derivs. I (X = O, or S(O)m wherein m is an integer from 0 to 2, or a substituted amine; R1 = alkyl, alkynyl, cycloalkyl, aryl heterocycle, halogen, alkoxy etc.; R2 = amino, acylamino, thioacylamino, carbamoyl, thiocarbamoyl, ureido, thioredio, sulfonamido, hydroxylamino, alkoxyamino, thioalkylamino, mercaptoamino, hydrazino, alkylhydrazino, aryl, heterocycle, etc.; R3, R4 = H, halogen, alkyl, alkenyl, alkynyl, alkyl, carboxy, acetoxy, alkoxy, oxyheterocyclic, etc.) their pharmaceutically acceptable salts, N-oxides, solvates, dihydro- and tetrahydro derivs. and enantiomers, for the manufacture of a medicament for the prevention or treatment of TNF-α related disorders. Thus, 2-amino-4-isopropoxypteridine was cooled in trifluoroacetic acid and treated with 35% H2O2 to give 2-amino-4-isopropoxypteridine-N8-oxide which had a IC50 value of 4.0 μM against TNF-α. The conditions treated may be septic or endotoxic shock, toxic effects of radiotherapy, TNF-α or chemotherapeutic agents, or cachexia.

IT 247913-51-5P 247913-54-8P 247913-56-0P
278799-96-5P 278800-02-5P 278800-27-4P
278800-23-6P 847832-39-7P 847832-40-0P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of pteridine derivs. for treating TNF-alpha related disorders)

RN 247913-51-5 HCAPLUS
CN 2,4-Pteridinediamine, N4,N4-dimethyl-6-phenyl- (CA INDEX NAME)



RN 247913-54-8 HCAPLUS
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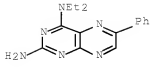

RN 247913-56-0 HCAPLUS
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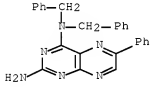

RN 278799-96-5 HCAPLUS
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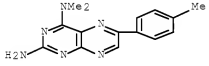

RN 278800-02-5 HCAPLUS
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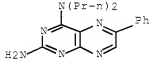
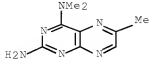
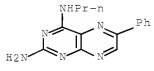


RN 278800-27-4 HCAPLUS
CN 2,4-Pteridinediamine, N4,N4,6-trimethyl- (CA INDEX NAME)



RN 278800-29-6 HCAPLUS
CN 2,4-Pteridinediamine, 6-phenyl-N4-propyl- (CA INDEX NAME)



RN 847832-39-7 HCAPLUS
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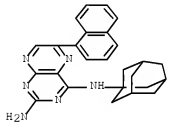

RN 847832-40-0 HCAPLUS
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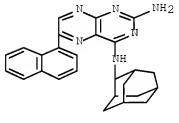

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L62 ANSWER 7 OF 215 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:216684 HCAPLUS Full-text
DOCUMENT NUMBER: 142:298130
TITLE: Preparation and immunosuppressive effects of pteridine derivatives
INVENTOR(S): Waer, Mark Jozef Albert; Herdewijn, Piet Andre Maurits Maria; Pfleiderer, Wolfgang Eugen; Marchand, Arnaud Didier Marie; De Jonghe, Steven Cesar Alfons
PATENT ASSIGNEE(S): 4 Aza Bioscience NV, Belg.
SOURCE: PCT Int. Appl., 100 pp.

CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 8
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE | |
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| WO 2005021003 | A2 | 20050310 | WO 2004-BE124 | 20040827 | <-- |
| WO 2005021003 | A3 | 20050609 | | | |
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| RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | | |
| US 2004077859 | A1 | 20040422 | US 2003-651604 | 20030829 | <-- |
| US 7276506 | B2 | 20071002 | | | |
| GB 2413324 | A | 20051026 | GB 2004-8955 | 20040422 | |
| AU 2004267885 | A1 | 20050310 | AU 2004-267885 | 20040827 | <-- |
| CA 2534151 | A1 | 20050310 | CA 2004-2534151 | 20040827 | <-- |
| EP 1658081 | A2 | 20060524 | EP 2004-761485 | 20040827 | <-- |
| EP 1658081 | B1 | 20071024 | | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK | | | | | |
| JP 2007533610 | T | 20071122 | JP 2006-524183 | 20040827 | |
| US 2006287314 | A1 | 20061221 | US 2006-595126 | 20060227 | <-- |
| PRIORITY APPLN. INFO.: | | | US 2003-651604 | A 20030829 | <-- |
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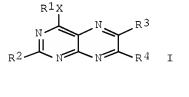
| | | | US 2001-869468 | B2 20011010 | <-- |
| | | | WO 2004-BE124 | W 20040827 | |

OTHER SOURCE(S): CASREACT 142:298130; MARPAT 142:298130
ED Entered STN: 11 Mar 2005
GI



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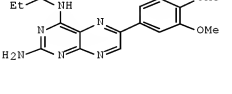


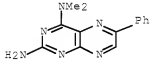
II

AB This invention relates to a group of trisubstituted and tetrasubstituted pteridine derivs. I [X = O, S(O)m, NZ; m = 0-2; Z = H, OH, R1 or NZ = heterocyclic group; R1 = (un)substituted C1-7 alkyl, C2-7 alkenyl, C2-7 alkynyl, C3-10 cycloalkyl, C3-10 cycloalkenyl, aryl, alkylaryl, arylalkyl, heterocyclyl, heterocycloalkyl, etc.; R2 = amino, acylamino, thioacylamino,

carbamoyl, thiocarbamoyl, ureido, thioureido, sulfonamido, hydroxylamino, alkoxyamino, thioalkylamino, hydrazino, etc.; R3 = F, Cl, Br, iodo, any group R1; R4 = H, halo, any group R1], their pharmaceutically acceptable salts, N-oxides, solvates, dihydro and tetrahydro derivs. and enantiomers, possessing unexpectedly desirable pharmaceutical properties, in particular which are highly active immunosuppressive agents, and as such are useful in the treatment in transplant rejection and/or in the treatment of certain inflammatory diseases. These compds. are also useful in preventing or treating cardiovascular disorders, allergic conditions, disorders of the central nervous system and cell proliferative disorders. Thus, (S)-sec-butylpteridine II (prepared in several steps from 2,6-diamino-5-hydroxypyrimidine, 3,4-dimethoxyphenylglyoxal oxime, and (S)-sec-butylamine) showed an IC50 of 0.2 μmol/L in a mixed lymphocyte suppression assay and an IC50 value of 0.3 μM in a TNF-α suppression assay.

IT 247913-51-5P 247913-54-8P 247913-56-0P
278799-96-5P 278800-02-5P 278800-20-7P
278800-22-9P 278800-24-1P 278800-27-4P
278800-29-6P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation and immunosuppressive effects of pteridine derivs.)

RN 247913-51-5 HCAPLUS
CN 2,4-Pteridinediamine, N4,N4-dimethyl-6-phenyl- (CA INDEX NAME)




RN 247913-54-8 HCAPLUS
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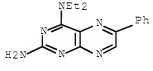
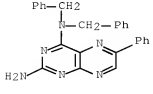



RN 247913-56-0 HCAPLUS
CN 2,4-Pteridinediamine, 6-phenyl-N4,N4-bis(phenylmethyl)- (CA INDEX NAME)



RN 278799-96-5 HCAPLUS
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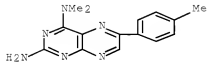


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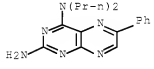


RN 278800-20-7 HCAPLUS
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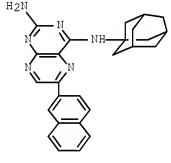
(CA INDEX NAME)




RN 278800-22-9 HCAPLUS
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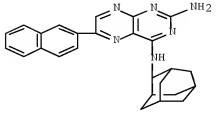
(CA INDEX NAME)



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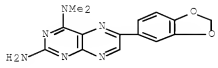
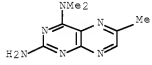


RN 278800-27-4 HCAPLUS
CN 2,4-Pteridinediamine, N4,N4,6-trimethyl- (CA INDEX NAME)



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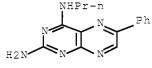

L62 ANSWER 8 OF 215 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:122801 HCAPLUS Full-text
DOCUMENT NUMBER: 142:198349
TITLE: Preparation of ornithine derivative ammonium salts for treating inflammatory diseases
INVENTOR(S): Rosenwald, Lindsay A.; Weiser, Michael; Stein, Jason; Serbin, Jeff
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 15 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| US 2005032807 | A1 | 20050210 | US 2003-634811 | 20030806 <-- |
| AU 2004264785 | A1 | 20050224 | AU 2004-264785 | 20040223 <-- |

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     WO 2005016350       A1    20050224    WO 2004-US5357         20040223 <--
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            GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
            LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
            NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
            TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
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            TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
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     JP 2007501227       T     20070125    JP 2006-522537         20040223 <--
     KR 2007029101       A     20070313    KR 2006-702558         20060206 <--
PRIORITY APPLN. INFO.:                      US 2003-634811      A  20030806 <--
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OTHER SOURCE(S):         CASREACT 142:198349; MARPAT 142:198349
ED   Entered STN:  11 Feb 2005
GI
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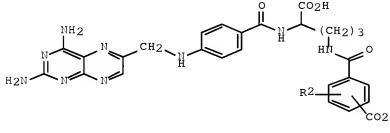

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AB   The invention relates to pharmaceutically-active ornithine compds.,
     particularly to pharmaceutically-acceptable ammonium salts of Nα-(4-amino-4-
     deoxypteroyl)-L-ornithine Nδ -acyl derivs. I [R2 is H, alk(en)(yn)yl,
     cycloalkyl, alkoxy, Cl, F, OH or CO2H (up to four groups)].  Thus, Nα-(4-
     amino-4-deoxypteroyl)-Nδ-hemiphthaloyl- L-ornithine ammonium salt was prepared
     by a multistep sequence starting with reaction of tetraaminopyrimidine sulfate
     with L-cysteine HCl salt and dihydroxyacetone dimer.  The ammonium salts
     provided by the invention exhibit chemical stability superior to that of
     corresponding acidic Nδ-acyl derivs. of Nα-(4-amino-4-deoxypteroyl)-L-
     ornithine compds.
IT   945-24-4P 100462-86-0P
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
     (Reactant or reagent)
        (preparation of ornithine derivative ammonium salts for treating
inflammatory
        diseases)
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CN   6-Pteridinemethanol, 2,4-diamino-  (CA INDEX NAME)
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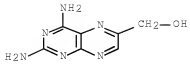
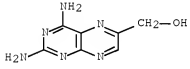


RN 100462-86-0 HCAPLUS
CN 6-Pteridinemethanol, 2,4-diamino-, hydrochloride (9CI) (CA INDEX NAME)



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L62 ANSWER 9 OF 215 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:331825 HCAPLUS Full-text
DOCUMENT NUMBER: 140:350561
TITLE: Immunosuppressive effects of pteridine derivatives and pharmaceutical compositions containing them
INVENTOR(S): Waer, Mark Jozef Albert; Herdewijn, Piet Andre Maurits Maria; Pfleiderer, Wolfgang Eugen
PATENT ASSIGNEE(S): 4 Aza Bioscience NV, Belg.
SOURCE: U.S. Pat. Appl. Publ., 46 pp., Cont.-in-part of U.S. Ser. No. 869,468, abandoned.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 8
PATENT INFORMATION:

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|---|---|---|---|---|
| US 2004077859 | A1 | 20040422 | US 2003-651604 | 20030829 <-- |
| US 7276506 | B2 | 20071002 | | |
| WO 2000039129 | A1 | 20000706 | WO 1999-EP10320 | 19991228 <-- |
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| RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| AU 2004267885 | A1 | 20050310 | AU 2004-267885 | 20040827 <-- |
| CA 2534151 | A1 | 20050310 | CA 2004-2534151 | 20040827 <-- |
| WO 2005021003 | A2 | 20050310 | WO 2004-BE124 | 20040827 <-- |
| WO 2005021003 | A3 | 20050609 | | |
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          LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
          NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
          TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
       RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
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          EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE,
          SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,
          SN, TD, TG
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    EP 1658081          B1    20071024
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    US 2006189620       A1    20060824    US 2006-275601          20060118 <--
    US 2006287314       A1    20061221    US 2006-595126          20060227 <--
PRIORITY APPLN. INFO.:                    US 1998-113989P     P   19981228 <--
                                          WO 1999-EP10320     W   19991228 <--
                                          US 2001-869468      B2  20011010 <--
                                          US 2003-651604      A   20030829 <--
                                          GB 2004-8955        A   20040422
                                          WO 2004-BE124       W   20040827
OTHER SOURCE(S):         MARPAT 140:350561
ED   Entered STN:  23 Apr 2004
AB   This invention relates to a group of trisubstituted and tetrasubstituted
     pteridine derivs., their pharmaceutically acceptable salts, N-oxides,
     solvates, dihydro- and tetrahydroderivatives and enantiomers, possessing
     unexpectedly desirable pharmaceutical properties, in particular which are
     highly active immunosuppressive agents, and as such are useful in the
     treatment in transplant rejection and/or in the treatment of certain
     inflammatory diseases.  These compds. are also useful in preventing or
     treating cardiovascular disorders, allergic conditions, disorders of the
     central nervous system and cell proliferative disorders.  The pteridine
     derivs. (preparation given) inhibited the mixed lymphocyte reaction and
     reduced T cell proliferation in the CD3 and CD28 assay.
IT   247913-51-5P 247913-54-8P 247913-56-0P
     278799-96-5P 278800-02-5P 278800-27-4P
     278800-29-6P
     RL: BSU (Biological study, unclassified); PAC (Pharmacological activity);
     SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological
     study); PREP (Preparation); USES (Uses)
        (immunosuppressant pteridine derivs. and compns.)
RN   247913-51-5  HCAPLUS
CN   2,4-Pteridinediamine, N4,N4-dimethyl-6-phenyl-  (CA INDEX NAME)
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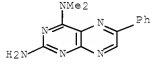


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RN   247913-54-8  HCAPLUS
CN   2,4-Pteridinediamine, N4,N4-diethyl-6-phenyl-  (CA INDEX NAME)
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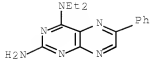
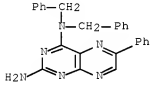


RN 247913-56-0 HCAPLUS
CN 2,4-Pteridinediamine, 6-phenyl-N4,N4-bis(phenylmethyl)- (CA INDEX NAME)



RN 278799-96-5 HCAPLUS
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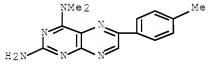
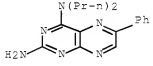
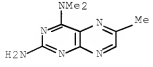


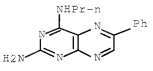
RN 278800-02-5 HCAPLUS
CN 2,4-Pteridinediamine, 6-phenyl-N4,N4-dipropyl- (CA INDEX NAME)



RN 278800-27-4 HCAPLUS
CN 2,4-Pteridinediamine, N4,N4,6-trimethyl- (CA INDEX NAME)



RN 278800-29-6 HCAPLUS
CN 2,4-Pteridinediamine, 6-phenyl-N4-propyl- (CA INDEX NAME)




L62 ANSWER 10 OF 215 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:312329 HCAPLUS Full-text
DOCUMENT NUMBER: 140:327052
TITLE: Pharmaceutically active ornithine derivatives, ammonium salts thereof and methods of making same
INVENTOR(S): Rosowsky, Andre; Bader, Henry; Blumbergs, Peter; Lin, Ming-Teh
PATENT ASSIGNEE(S): Dana-Farber Cancer Institute, USA; Ash Stevens, Inc.
SOURCE: U.S. Pat. Appl. Publ., 19 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE | |
|---|---|---|---|---|---|
| US 2004072837 | A1 | 20040415 | US 2003-412279 | 20030414 | <-- |
| US 6989386 | B2 | 20060124 | | | |
| AU 2004232668 | A1 | 20041104 | AU 2004-232668 | 20040223 | <-- |
| CA 2522538 | A1 | 20041104 | CA 2004-2522538 | 20040223 | <-- |
| WO 2004094427 | A1 | 20041104 | WO 2004-US5356 | 20040223 | <-- |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | | |
| RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | | |
| EP 1638973 | A1 | 20060329 | EP 2004-713766 | 20040223 | <-- |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, SK | | | | | |
| BR 2004009441 | A | 20060418 | BR 2004-9441 | 20040223 | <-- |
| JP 2006523689 | T | 20061019 | JP 2006-508804 | 20040223 | <-- |
| MX 2005PA10957 | A | 20060418 | MX 2005-PA10957 | 20051012 | <-- |
| NO 2005005311 | A | 20060110 | NO 2005-5311 | 20051110 | <-- |
| IN 2005CN02989 | A | 20070727 | IN 2005-CN2989 | 20051114 | <-- |
| US 2006079531 | A1 | 20060413 | US 2005-286126 | 20051122 | <-- |
| US 2007219204 | A1 | 20070920 | US 2006-417479 | 20060427 | <-- |

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|---|---|---|---|---|
| PRIORITY APPLN. INFO.: | | US 2002-376615P | P | 20020430 <-- |
| | | US 2003-412279 | A | 20030414 <-- |
| | | WO 2004-US5356 | W | 20040223 |
| | | US 2005-286126 | A1 | 20051122 |

OTHER SOURCE(S): MARPAT 140:327052

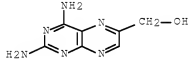
ED Entered STN: 16 Apr 2004

AB The present invention relates to pharmaceutically active ornithine compds., particularly to pharmaceutically acceptable ammonium salts of Nδ-acyl derivs. of Nα(4-amino-4-deoxypteroyl)-L-ornithine compds.; and methods of treatment and pharmaceutical compns. that utilize or comprise one or more of such ammonium salts. The ammonium salts provided by the invention exhibit superior chemical stability than corresponding acidic Nδ-acyl derivs. of Nα(4-amino-4-deoxypteroyl)-L-ornithine compds. Thus, Nδ-(4-amino-4- deoxypteroyl)Nδ-hemiphthaloyl-L-ornithine ammonium salt was prepd by the reaction of Nδ-phthaloyl-L-ornithine with ammonium hydroxide solution as a yellow powder (yield = 93%).

IT 945-24-4, 2,4-Diamino-6-hydroxymethylPteridine
RL: RCT (Reactant); RACT (Reactant or reagent)
(pharmaceutically active ornithine derivs., ammonium salts thereof and methods of making same)

RN 945-24-4 HCAPLUS

CN 6-Pteridinemethanol, 2,4-diamino- (CA INDEX NAME)



REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L62 ANSWER 100 OF 215 HCAPLUS COPYRIGHT 2007 ACS on STN

| | |
|---|---|
| ACCESSION NUMBER: | 1985:487712 HCAPLUS Full-text |
| DOCUMENT NUMBER: | 103:87712 |
| ORIGINAL REFERENCE NO.: | 103:14085a,14088a |
| TITLE: | 2-(2,4-Diamino-6-pteridinyl)vinylbenzene derivatives |
| INVENTOR(S): | Piper, James R.; Montgomery, John A. |
| PATENT ASSIGNEE(S): | Southern Research Institute, Australia |
| SOURCE: | Pat. Specif. (Aust.), 11 pp.<br>CODEN: ALXXAP |
| DOCUMENT TYPE: | Patent |
| LANGUAGE: | English |
| FAMILY ACC. NUM. COUNT: | 1 |

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| AU 541315 | B2 | 19850103 | AU 1981-73914 | 19810807 <-- |
| AU 8173914 | A | 19811112 | | |
| PRIORITY APPLN. INFO.: | | | AU 1981-73914 | 19810807 <-- |

OTHER SOURCE(S): CASREACT 103:87712

ED Entered STN: 22 Sep 1985

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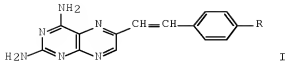
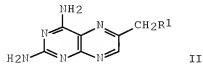


I



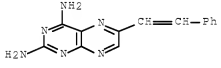
II

AB The title compds. I (R = H, CO2H, alkoxycarbonyl, esterified glutamyl) were prepared Thus, bromomethylpteridine II (R1 = Br) was treated with PPh3 to give II (R1 = P+Ph3 Br-) which was converted to the ylide and treated with di-Et 4-formylbenzoyl-L-glutamate to give I [R = CONHCH(CO2Et)CH2CH2CO2Et]. The latter compound was hydrogenated to 10-deazaaminopterin.

IT 50691-66-2P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 50691-66-2 HCAPLUS

CN 2,4-Pteridinediamine, 6-(2-phenylethenyl)- (CA INDEX NAME)



L62 ANSWER 101 OF 215 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1985:209260 HCAPLUS Full-text

DOCUMENT NUMBER: 102:209260

ORIGINAL REFERENCE NO.: 102:32733a,32736a

TITLE: Ammonia and methane chemical ionization mass spectra of methotrexate and its amide and ester analogs

AUTHOR(S): Cheung, H. T. Andrew; Tattam, Bruce N.; Antonjuk, David J.; Boadle, Deborah K.

CORPORATE SOURCE: Dep. Pharm., Univ. Sydney, Sydney, Australia

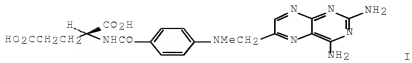
SOURCE: Biomedical Mass Spectrometry (1985), 12(1), 11-18
CODEN: BMSYAL; ISSN: 0306-042X

DOCUMENT TYPE: Journal

LANGUAGE: English

ED Entered STN: 15 Jun 1985

GI



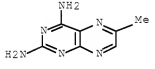
I

AB The use of chemical-ionization mass spectrometry for the characterization of analogs of methotrexate (I) [59-05-2] was studied. With CH4 [74-82-8] as reactant gas, abundant [MH]+ ions were generally not produced. However, with NH3, especially in conjunction with thermal desorption from a Pt wire, significant amts. of [MH]+ ions were formed by I the α- [71074-47-0], γ- [64801-56-5] and diamide [62703-30-4] analogs, and a series of α- and γ- monoalkylamide derivs. The tert-Bu esters of the various monoamides behaved similarly to the corresponding monoamides, except for the ready loss of isobutylene. Fragment ions from both CH4 and NH3 chemical ionization were formed by cleavages benzylic to the pteridine ring, by bond breakage at the amide bond between the aminobenzoyl and glutamyl moieties, and by fragmentations on both sides of this amide bond. Fragment ions from these processes, in conjunction with further disintegration of the glutamyl moiety, are diagnostic of the structures of the pteridine, amminobenzoyl and glutamyl moieties of the analogs. Examples of application to structural determination are given.

IT 708-74-7
RL: PRP (Properties)
(chemical-ionization mass spectroscopy of, ammonia or methane reactants in)

RN 708-74-7 HCAPLUS

CN 2,4-Pteridinediamine, 6-methyl- (CA INDEX NAME)



L62 ANSWER 102 OF 215 HCAPLUS COPYRIGHT 2007 ACS on STN

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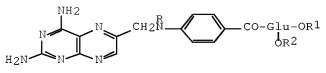
|---|---|
| ACCESSION NUMBER: | 1985:167139 HCAPLUS Full-text |
| DOCUMENT NUMBER: | 102:167139 |
| ORIGINAL REFERENCE NO.: | 102:26301a,26304a |
| TITLE: | Methotrexate analogs. 25. Chemical and biological studies on the γ-tert-butyl esters of methotrexate and aminopterin |
| AUTHOR(S): | Rosowsky, Andre; Freisheim, James H.; Bader, Henry; Forsch, Ronald A.; Susten, Sandra A.; Cucchi, Carol A.; Frei, Emil, III |
| CORPORATE SOURCE: | Dana-Farber Cancer Inst., Harvard Med. Sch., Boston, MA, 02115, USA |
| SOURCE: | Journal of Medicinal Chemistry (1985), 28(5), 660-7<br>CODEN: JMCMAR; ISSN: 0022-2623 |
| DOCUMENT TYPE: | Journal |
| LANGUAGE: | English |

OTHER SOURCE(S): CASREACT 102:167139
ED Entered STN: 18 May 1985
GI



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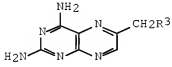
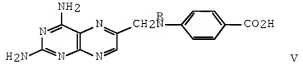


IV



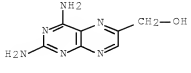
V

AB γ-tert-Bu aminopterin (I; R = R1 = H, R2 = CMe3) (II) was prepared, and new routes to the known γ-tert-Bu methotrexate (I; R = Me, R1 = H, R2 = CMe3) (III) were developed. Thus, pteridine IV (R3 = OH) was brominated by Br2/PPh3 to give IV (R3 = Br), which was treated in situ with p-H2NC6H4CO2H to give pteroic acid V (R = H), which was formylated to give V (R = CHO). The latter was condensed with H-Glu(OCMe3)-OMe.HCl by ClCO2CH2CHMe2 in DMF containing Et3N to give I (R = CHO, R1 = Me, R2 = CMe3), which was hydrolyzed and then deformylated to give II. II was also prepared by treating IV.HBr (R3 = Br) with p-RNHC6H4CO-Glu(OCMe3)-OR1 (VI, R = R1 = H) in AcNMe2 containing Me2CHNEt2. III was prepared by brominating IV (R3 = OH), treating the resulting IV (R3 = Br) with VI (R = R1 = Me), and hydrolyzing the resulting I (R = R1 Me, R2 = CMe3). The inhibitory effects of II on the activity of dihydrofolate reductase (DHFR) from L1210 murine leukemia cells, the growth of 4210 cells and CEM human leukemic lymphoblasts in suspension culture, and the growth of human squamous cell carcinoma of the head and neck in monolayer culture were compared with the effects of III and the parent acids aminopterin (I, R-R2 = H) and methotrexate (I, R = Me, R1 = R2 = H). The activity of II was close to that of III in the DHFR inhibition assay, but II was more potent than III against cells in culture and against L1210 leukemia in mice.

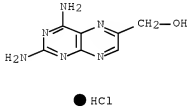
IT 945-24-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and bromination of)

RN 945-24-4 HCAPLUS

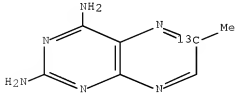
CN 6-Pteridinemethanol, 2,4-diamino- (CA INDEX NAME)



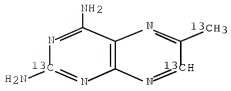
IT 73978-41-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and neutralization of)
RN 73978-41-3 HCAPLUS
CN 6-Pteridinemethanol, 2,4-diamino-, hydrochloride (1:1) (CA INDEX NAME)



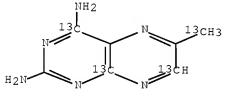
L62 ANSWER 103 OF 215 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1985:6425 HCAPLUS Full-text
DOCUMENT NUMBER: 102:6425
ORIGINAL REFERENCE NO.: 102:1167a,1170a
TITLE: Multi-carbon-13-labeled 2,4-diamino-6-methylpteridine
AUTHOR(S): Cheung, H. T. A.; Gray, P. G.
CORPORATE SOURCE: Dep. Pharm., Univ. Sydney, Sydney, Australia
SOURCE: Journal of Labelled Compounds and Radiopharmaceuticals (1984), 21(5), 471-83
CODEN: JLCRD4; ISSN: 0362-4803
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 12 Jan 1985
AB Samples of 2,4-diamino-6-methylpteridine (I) specifically labeled with 13C at 1 or more positions were prepared and characterized by 1H and 13C NMR. E.g., treatment of 2,4,5,6-tetraaminopyrimidine with NaHSO3 and Me13COCHCl2 under pH-controlled conditions gave I-6-13C in 41% yield.
IT 93665-13-5P 93665-14-6P 93665-15-7P
93665-16-8P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 93665-13-5 HCAPLUS
CN 2,4-Pteridinediamine-6-13C, 6-methyl- (9CI) (CA INDEX NAME)



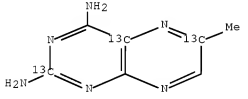
RN 93665-14-6 HCAPLUS
CN 2,4-Pteridinediamine-2,7-13C2, 6-(methyl-13C)- (9CI) (CA INDEX NAME)



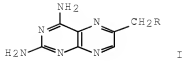
RN 93665-15-7 HCAPLUS
CN 2,4-Pteridinediamine-4,7,8a-13C3, 6-(methyl-13C)- (9CI) (CA INDEX NAME)



RN 93665-16-8 HCAPLUS
CN 2,4-Pteridinediamine-2,4a,6-13C3, 6-methyl- (9CI) (CA INDEX NAME)



L62 ANSWER 104 OF 215 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1984:630476 HCAPLUS Full-text
DOCUMENT NUMBER: 101:230476
ORIGINAL REFERENCE NO.: 101:35001a,35004a
TITLE: Synthesis of 2,4-diamino-6-substituted pteridine
AUTHOR(S): Shey, Chun Feng; Chen, Chao Tung; Horng, Jhy Ming; Wang, Cheng Hsia
CORPORATE SOURCE: Dep. Chem., Natl. Taiwan Norm. Univ., Taipei, Taiwan
SOURCE: Shida Xuebao (Taipei) (1984), 29, 631-43
CODEN: STHPD8; ISSN: 0583-0249
DOCUMENT TYPE: Journal
LANGUAGE: Chinese
ED Entered STN: 22 Dec 1984
GI



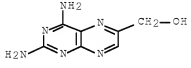
I

AB Title compds. I (R = Cl, OH), intermediates for methotrexate, were prepared Thus, cyclocondensation of 2,4,5,6-tetraaminopyrimidine with CO(CH2OH)2 gave I (R = OH) whereas cyclocondensation of 2-amino-3-cyano-5- chloromethylpyrazine with guanidine gave I (R = Cl).

IT 945-24-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and chlorination of)

RN 945-24-4 HCAPLUS

CN 6-Pteridinemethanol, 2,4-diamino- (CA INDEX NAME)



L62 ANSWER 105 OF 215 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1984:622096 HCAPLUS Full-text

DOCUMENT NUMBER: 101:222096

ORIGINAL REFERENCE NO.: 101:33507a,33510a

TITLE: Functional group contributions to drug-receptor interactions

AUTHOR(S): Andrews, P. R.; Craik, D. J.; Martin, J. L.

CORPORATE SOURCE: Victorian Coll. Pharm. Ltd., Parkville, 3052, Australia

SOURCE: Journal of Medicinal Chemistry (1984), 27(12), 1648-57
CODEN: JMCMAR; ISSN: 0022-2623

DOCUMENT TYPE: Journal

LANGUAGE: English

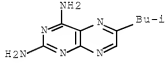
ED Entered STN: 22 Dec 1984

AB To overcome the difficulties in estimating the potential bond strengths involved in the interaction between a drug and a reasonable matched receptor, 200 drugs and enzyme inhibitors chosen on the basis of their apparent tight binding to their corresponding receptor sites, were used to provide a statistical estimate of the strength of noncovalent bonds associated with each functional groups in an average drug-receptor environment. Values are presented to determine the goodness of fit of a drug to its receptor by comparing the observed binding constant to the average binding energy calculated by summing the intrinsic binding energies of the component groups and then subtracting 2 entropy related terms. Drugs such as diazepam [439-14-5] that match their receptors well have a measured binding energy exceeding the calculated average value, whereas others such as buprenorphine [52485-79-7] who match their receptor less than the average have binding energies less the calculated average value. In addition the binding energies of 3 central

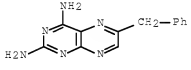
nervous system active drugs and representative amino acids within a polypeptide mol. are also given. General principles for the application of intrinsic binding energies in drug design and structure-activity relations are discussed.

IT 51395-54-1 51583-02-9
RL: PROC (Process)
(binding of, with receptors)

RN 51395-54-1 HCAPLUS
CN 2,4-Pteridinediamine, 6-(2-methylpropyl)- (CA INDEX NAME)




RN 51583-02-9 HCAPLUS
CN 2,4-Pteridinediamine, 6-(phenylmethyl)- (CA INDEX NAME)

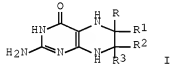



L62 ANSWER 106 OF 215 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1984:571289 HCAPLUS Full-text
DOCUMENT NUMBER: 101:171289
ORIGINAL REFERENCE NO.: 101:25911a,25914a
TITLE: Pteridines
PATENT ASSIGNEE(S): Wellcome Foundation Ltd., UK
SOURCE: Jpn. Kokai Tokkyo Koho, 16 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| JP 59076086 | A | 19840428 | JP 1983-172861 | 19830919 <-- |
| JP 05033229 | B | 19930519 | | |
| DK 8304260 | A | 19840321 | DK 1983-4260 | 19830919 <-- |
| AU 8319256 | A | 19840329 | AU 1983-19256 | 19830919 <-- |
| AU 572792 | B2 | 19880519 | | |
| EP 108890 | A2 | 19840523 | EP 1983-109291 | 19830919 <-- |
| EP 108890 | A3 | 19851002 | | |
| EP 108890 | B1 | 19881207 | | |
| R: BE, CH, DE, FR, GB, IT, LI, NL, SE | | | | |
| ZA 8306957 | A | 19850424 | ZA 1983-6957 | 19830919 <-- |
| CA 1288099 | C | 19910827 | CA 1983-437101 | 19830920 <-- |
| DK 8401591 | A | 19850113 | DK 1984-1591 | 19840319 <-- |

| | | | | | | |
|---|---|---|---|---|---|---|
| DK 161326 | B | 19910624 | | | | |
| DK 161326 | C | 19911209 | | | | |
| US 4587340 | A | 19860506 | US 1984-620152 | | 19840613 | <-- |
| US 4701455 | A | 19871020 | US 1985-747671 | | 19850621 | <-- |
| US 4665182 | A | 19870512 | US 1985-799285 | | 19851119 | <-- |
| PRIORITY APPLN. INFO.: | | | GB 1982-26688 | A | 19820920 | <-- |
| | | | GB 1983-18833 | A | 19830712 | <-- |
| | | | US 1983-533785 | A1 | 19830919 | <-- |
| | | | US 1983-533786 | A | 19830919 | <-- |

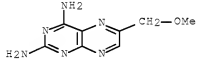
OTHER SOURCE(S): MARPAT 101:171289
ED Entered STN: 10 Nov 1984
GI



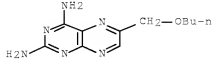
I

AB The title compds. I [R,R1 = H, (substituted) alkyl; R2,R3 = H, alkyl] were prepared Thus, 2,4-diamino-6-(methoxymethyl)pteridine, obtained via reaction of 2-amino-3-cyano-5-(methoxymethyl)pyrazine with formamidine, was hydrolyzed in 1 N NOH at 70° for 3 h to give 83% 2-amino-6-(methoxymethyl)-4(3H)-pteridine, hydrogenation of which gave 85% I (R = MeOCH2, R1-R3 = H). The antidepressant, antihypotensive, and anti-Parkinsonism activities of I were measured by their effects on various enzymes.

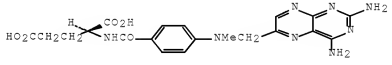
IT 40110-13-2P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and hydrazolysis of)
RN 40110-13-2 HCAPLUS
CN 2,4-Pteridinediamine, 6-(methoxymethyl)- (CA INDEX NAME)



IT 92530-52-4P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 92530-52-4 HCAPLUS
CN 2,4-Pteridinediamine, 6-(butoxymethyl)- (CA INDEX NAME)



L62 ANSWER 107 OF 215 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1983:590715 HCAPLUS Full-text
DOCUMENT NUMBER: 99:190715
ORIGINAL REFERENCE NO.: 99:29291a,29294a
TITLE: Photosensitization by methotrexate photoproducts
AUTHOR(S): Chahidi, C.; Morliere, P.; Aubailly, M.; Dubertret, L.; Santus, R.
CORPORATE SOURCE: Lab. Phys. Chim. Adapt. Biol., Mus. Natl. Hist. Nat., Paris, 75231, Fr.
SOURCE: Photochemistry and Photobiology (1983), 38(3), 317-22
CODEN: PHCBAP; ISSN: 0031-8655
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 12 May 1984
GI



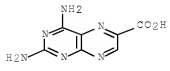
I

AB Photoproducts induced upon excitation of methotrexate (I) by UV light have been separated by ion-exchange chromatog. They include 2,4-diamino-6-pteridinecarboxylic acid, 2,4-diamino-6-pteridinecarboxaldehyde, and other unidentified pteridine derivs. The same photoproducts can be also formed upon photodynamic reaction using hematoporphyrin as photosensitizer. In O-saturated aqueous solns. (pH.apprx.7), I photoproducts sensitize the oxidation of histidine and tryptophan by UV light by a process involving singlet O. In aqueous solns. containing albumin or in human serum, the same photoproducts are formed from free I but not from albumin-bound I. In the latter case, the results may suggest that I covalently binds to albumin upon excitation with UV light either in the absence or in presence of O. These results could explain the photosensitization accompanying cancer chemotherapy with high dose I and also the synergistic effects of psoralen + UVA + low dose I in psoriasis therapy.

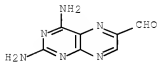
IT 716-74-5 4261-17-0
RL: BIOL (Biological study)
(as methotrexate photoproduct, photosensitization by)

RN 716-74-5 HCAPLUS

CN 6-Pteridinecarboxylic acid, 2,4-diamino- (CA INDEX NAME)



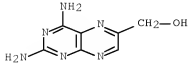
RN 4261-17-0 HCAPLUS
CN 6-Pteridinecarboxaldehyde, 2,4-diamino- (CA INDEX NAME)



L62 ANSWER 108 OF 215 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1983:454148 HCAPLUS Full-text
DOCUMENT NUMBER: 99:54148
ORIGINAL REFERENCE NO.: 99:8473a,8476a
TITLE: Separation of triphenylphosphine oxide from methotrexate ester and purification of this ester
INVENTOR(S): Ellard, James A.; Webster, James A.
PATENT ASSIGNEE(S): United States Dept. of Health and Human Services, USA
SOURCE: U. S. Pat. Appl., 10 pp. Avail. NTIS Order No. PAT-APPL-6-329 869
CODEN: XAXXAV
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

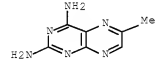
| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| US 329869 | A0 | 19830318 | US 1981-329869 | 19811211 <-- |
| US 4421913 | A | 19831220 | | |
| US 143129 | A0 | 19810327 | US 1980-143129 | 19800423 <-- |
| PRIORITY APPLN. INFO.: | | | US 1980-143129 | 19800423 <-- |

OTHER SOURCE(S): CASREACT 99:54148
ED Entered STN: 12 May 1984
AB The Ph3PO generated by hydrolysis of the protective groups in the synthesis of methotrexate was separated from the reaction mixture by extraction with toluene or BTX-type solvents. Also, the methotrexate ester was purified by a procedure which involved filtering an acidic EtOH solution of the ester.
IT 76145-91-0
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with di-Et [(methylamino)benzoyl]glutamine)
RN 76145-91-0 HCAPLUS
CN 6-Pteridinemethanol, 2,4-diamino-, hydrobromide (9CI) (CA INDEX NAME)



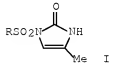
x HBr

L62 ANSWER 109 OF 215 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1983:224048 HCAPLUS Full-text
DOCUMENT NUMBER: 98:224048
ORIGINAL REFERENCE NO.: 98:33931a,33934a
TITLE: Electrochemistry of methotrexate. Part I. Characteristics of reduction
AUTHOR(S): Gurira, R. C.; Bowers, L. D.
CORPORATE SOURCE: Dep. Lab. Med. Pathol., Univ. Minnesota, Minneapolis, MN, 55455, USA
SOURCE: Journal of Electroanalytical Chemistry and Interfacial Electrochemistry (1983), 146(1), 109-22
CODEN: JEIEBC; ISSN: 0022-0728
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 12 May 1984
AB The electrochem. reduction of methotrexate (MTX) [59-05-2] was studied in the pH range of 2 to 11. Methotrexate exhibits 3 two-electron/two-proton reduction steps in neutral and acidic media. Based on the results of cyclic voltammetry and high performance liquid chromatog. anal. of the products formed in controlled potential electrolysis, the 1st reduction produces 5,8-dihydro-MTX [86011-02-1] which undergoes either a heretofore unreported proton-dependent cleavage or proton-dependent tautomerization to 7,8-dihydro-MTX [14009-31-5]. The rate constant for the tautomerization was pH dependent and varied from 0.41 s-1 to 0.019 s-1 in the pH range of 3.5 to 7.6. The 2nd reduction cleaves the C(9)-N(10) bond of the 7,8--dihydro-MTX. The final reduction produces a 5,6,7,8-tetrahydro derivative of the substituted pteridine. In alkaline media, a single two-electron/two- proton reduction is observed due to the very slow tautomerization process required to produce the reactant for subsequent redns.
IT 708-74-7P
RL: FORM (Formation, nonpreparative); PREP (Preparation)
(formation of, in electrochem. reduction of methotrexate)
RN 708-74-7 HCAPLUS
CN 2,4-Pteridinediamine, 6-methyl- (CA INDEX NAME)




L62 ANSWER 110 OF 215 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1982:616120 HCAPLUS Full-text
DOCUMENT NUMBER: 97:216120
ORIGINAL REFERENCE NO.: 97:36277a,36280a
TITLE: Reactions of tetraaminopyrimidine with 1-arylsulfonyl-4-methylimidazolin-2-ones
AUTHOR(S): Zav'yalov, S. I.; Zavozin, A. G.
CORPORATE SOURCE: Inst. Org. Khim. im. Zelinskogo, Moscow, USSR
SOURCE: Izvestiya Akademii Nauk SSSR, Seriya Khimicheskaya (1982), (8), 1910-13
CODEN: IASKA6; ISSN: 0002-3353
DOCUMENT TYPE: Journal

LANGUAGE: Russian
OTHER SOURCE(S): CASREACT 97:216120
ED Entered STN: 12 May 1984
GI

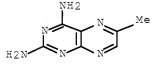


I

AB Cyclocondensation of 2,4,5,6-tetraaminopyrimidine with I (R = 4-MeOC6H4, 4-FC6H4, 2,5-Cl2C6H3, 2,5-Br2C6H3, 4-BrC6H4, 4-O2NC6H4) yields 6-methyl-2,4-diaminopteridine of the aryl group contains an electron donating substituent and 7-methyl-2,4-diaminopteridine when the substituent is an electron-accepting group.

IT 708-74-7P
RL: FORM (Formation, nonpreparative); PREP (Preparation)
(formation of, in cyclocondensation of (arylsulfonyl)methylimidazolinones with tetraaminopyrimidine)

RN 708-74-7 HCAPLUS
CN 2,4-Pteridinediamine, 6-methyl- (CA INDEX NAME)



L62 ANSWER 205 OF 215 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1955:8559 HCAPLUS
DOCUMENT NUMBER: 49:8559
ORIGINAL REFERENCE NO.: 49:1825i,1826a-e
TITLE: 2,4-Diaminopteridine aldehydes
INVENTOR(S): Petering, Harold G.
PATENT ASSIGNEE(S): Upjohn Co.
DOCUMENT TYPE: Patent
LANGUAGE: Unavailable
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| US 2667484 | | 19540126 | US 1950-175476 | 19500722 <-- |

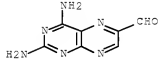
ED Entered STN: 22 Apr 2001

AB Oxidation with Pb(OAc)4 or HIO4 of 2,4-diamino-6 (and 7)-(polyhydroxyalkyl)pteridines gave the corresponding formyl derivs. Thus, to 2,4-diamino-6-(tetrahydroxybutyl)pteridine (I) 1.41 g. and 25% aqueous HOAc 75 ml. was added Pb3O4 10.3 g. portionwise over a period of 0.5 hr., the mixture allowed to stand 20 min. (during which time the temperature rose to 40° and all the Pb3O4 had gone into solution), treated with activated C 200 mg., stirred, allowed to stand 15 min., filtered, the filtrate treated with (NH4)2SO4 6 g. in H2O 15 ml., the precipitate of PbSO4 filtered, and the filtrate divided into 2 portions. One portion was extracted twice with Et2O 250 ml., and the yellow precipitate formed in the cooled aqueous layer collected, washed with EtOH, then Me2CO and Et2O, giving 70 mg. 2,4-diamino-6-formylpteridine (II), absorption maximum in 0.1N NaOH at 262 and 370 mμ, min. at 315 mμ. The pH of the 2nd portion adjusted to 5.0 with Na2CO3 yielded 65 mg. II which was washed as above. It was possible to isolate by standard procedures 180 mg. II phenylhydrazone from the combined mother liquors of both portions. Also reported are the following derivs. of II (ultraviolet maximum and min. as mμ in parentheses): thiosemicarbazone (265, 340, and 405; 245, 305, and 370); oxime (262, and 382; 342 and 240, point of inflection about 305); also 2,4-diamino-7-formylpteridine (258 and 370; 236 and 310). I was prepared as follows: H2O 13 ml. and then HOAc 1 ml. and 85% N2- H4.H2O 0.6 ml. were added in that order to a dry mixture of 2,4,5,6-tetraaminopyrimidine-2HCl 1.065 g., NaHCO3 0.85 g., and L-sorbose 1.8 g., the pH adjusted from about 7.0 to 5-6 with glacial HOAc (about 0.5 ml.), the mixture heated 2 hrs. on a H2O bath at 95-100°, cooled 16 hrs. at 5°, and the brown precipitate collected, washed with EtOH, Me2CO, and Et2O, and dried, yielding 0.67 g. I; diboric acid complex. Similarly prepared were the following 2,4-diaminopteridines: 6-trihydroxypropyl, 7-tetrahydroxybutyl, maximum in 0.1N NaOH, 235 and 310 mμ, min. 255 and 365 mμ; in 0.1N HCl, maximum at 240, 285, and 335 mμ, and 7-trihydroxypropyl. The aldehydes are valuable as intermediates in the synthesis of folic acid antagonists and related compds. The position of the formyl group was determined by an empirical spectral method. Cf. C.A. 46, 5094h.

IT 4261-17-0, 6-Pteridinecarboxaldehyde, 2,4-diamino- (and derivs.)

RN 4261-17-0 HCAPLUS

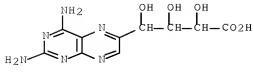
CN 6-Pteridinecarboxaldehyde, 2,4-diamino- (CA INDEX NAME)



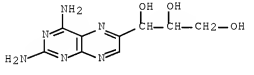

IT 36093-91-1P, 6-Pteridinebutyric acid, 2,4-diamino-α,β,γ-trihydroxy- 859055-16-6P, Pteridine, 2,4-diamino-6-(1,2,3-trihydroxypropyl)- 883310-60-9P, 1,2,3,4-Butanetetrol, 1-(2,4-diamino-6-pteridyl)-, L-xylo- 911667-16-8P, Pteridine, 2,4-diamino-6-L-xylo-tetrahydroxybutyl- RL: PREP (Preparation) (preparation of)

RN 36093-91-1 HCAPLUS

CN 6-Pteridinebutanoic acid, 2,4-diamino-α,β,γ-trihydroxy- (CA INDEX NAME)

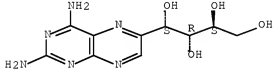


RN 859055-16-6 HCAPLUS
CN INDEX NAME NOT YET ASSIGNED



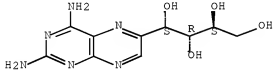
RN 883310-60-9 HCAPLUS
CN 1,2,3,4-Butanetetrol, 1-(2,4-diamino-6-pteridyl)-, L-xylo- (5CI) (CA INDEX NAME)

Relative stereochemistry.



RN 911667-16-8 HCAPLUS
CN INDEX NAME NOT YET ASSIGNED

Absolute stereochemistry.



L62 ANSWER 206 OF 215 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1954:77767 HCAPLUS
DOCUMENT NUMBER: 48:77767
ORIGINAL REFERENCE NO.: 48:13732e-g
TITLE: Isolation of 2,4-diaminopteridines
INVENTOR(S): Schmitt, John A.

PATENT ASSIGNEE(S): Upjohn Co.
DOCUMENT TYPE: Patent
LANGUAGE: Unavailable
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

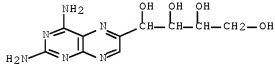
| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| US 2647898 | | 19530804 | US 1950-175480 | 19500722 <-- |

ED Entered STN: 22 Apr 2001

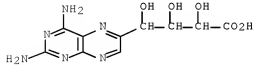
AB The yields in the isolation of 2,4-diaminopteridines from aqueous solns. are greatly increased by the use of boric acid (I) in the presence of sulfate ion. To a dry mixture containing 530 mg. 2,4,5,6-tetraaminopyridine-HCl (II), 900 mg. L-sorbose (III), 680 mg. AcONa.3H2O (IV), and 300 mg. I is added 0.3 ml. of 85% N2H4.3H2O (V) and 0.7 ml. glacial AcOH in 6.5 ml. H2O, the mixture warmed about 2 hrs. at 70°, the small amount of solid filtered off, and the pH adjusted to about 7 with NH4OH, the solution cooled 16 hrs. at about 5°, then warmed to room temperature, treated with 300 mg. I and 660 mg. (NH4)2SO4 (VI), cooled and the precipitated solid collected, washed with H2O, Me2CO, and ether, and dried at 60° in vacuo to give 430 mg. of the boric acid complex of 2,4-diamino-6-(tetrahydroxybutyl)pteridine (VII). When I is used in the absence of sulfate ion with the same amts. of reactants, only 50 mg. VII is obtained. If I is omitted, no pteridine is isolated.

IT 36093-90-0P, 1,2,3,4-Butanetetrol, 1-(2,4-diamino-6-pteridyl)-
36093-91-1P, 6-Pteridinebutyric acid, 2,4-diamino-
α,β,γ-trihydroxy- 854462-87-6P,
1,2,3,4-Butanetetrol, 1-(2,4-diamino-6-pteridyl)-, compound with boric acid
RL: PREP (Preparation)
(preparation of)

RN 36093-90-0 HCAPLUS
CN 1,2,3,4-Butanetetrol, 1-(2,4-diamino-6-pteridinyl)- (CA INDEX NAME)



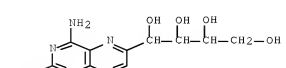
RN 36093-91-1 HCAPLUS
CN 6-Pteridinebutanoic acid, 2,4-diamino-α,β,γ-trihydroxy-
(CA INDEX NAME)



RN 854462-87-6 HCAPLUS
CN 1,2,3,4-Butanetetrol, 1-(2,4-diamino-6-pteridyl)-, compd. with boric acid
(5CI) (CA INDEX NAME)

CM 1

CRN 36093-90-0
CMF C10 H14 N6 O4



CM 2

CRN 10043-35-3
CMF B H3 O3

L62 ANSWER 207 OF 215 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1954:60630 HCAPLUS
DOCUMENT NUMBER: 48:60630
ORIGINAL REFERENCE NO.: 48:10787e-i
TITLE: 6-(Phenoxymethyl)pteridines
INVENTOR(S): Weisblat, David I.; Magerlein, Barney J.
PATENT ASSIGNEE(S): Upjohn Co.
DOCUMENT TYPE: Patent
LANGUAGE: Unavailable
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| US 2656356 | | 19531020 | US 1951-212668 | 19510224 <-- |

ED Entered STN: 22 Apr 2001
GI For diagram(s), see printed CA Issue.
AB Compds. having the general formula are described where each Z can be H, HO, HS, H2N, halogen, or alkyl, and Y can be H, O2N, H2N, halogen, alkyl, HO, RO, SO3H, CO2H, and esters or amides of the SO3H and CO2H groups. These compds. decompose above 300° and are best characterized by ultraviolet absorption spectra. They are useful as folic acid antagonists and differ in that their action is reversed, usually quantitatively, by administration of more folic acid; they are also useful as antiviral agents and as enzyme inhibitors. Their synthesis is best accomplished by interaction of YC6H4OCH2COCH(OR)2, where Y is as before, in glacial HOAc and an aqueous solution of freshly prepared 4,5-diaminopyrimidine in an inert atmospheric in the dark for 30-120 min. with heating. Thus, 0.8 g. p-(EtO)2CHCOCH2OC6H4CO2Et (preparation given) in 14.8 ml. glacial HOAc was added to a mixture of 0.42 g. NaOAc and 0.55 g.

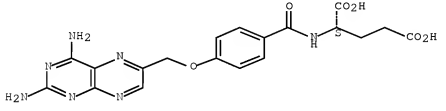
2,4,5-triamino-6- hydroxypyrimidine-2HCl, the mixture stirred 30 min. at room temperature in the dark under N, heated to 118-20°, stirred 20 min. longer, cooled to 0°, the dark precipitate collected, washed twice with H2O and once with Me2CO, and dried gave 0.58 g. Et 4-(2-amino-4-hydroxy-6-pteridyl)methoxybenzoate [2-amino-4-hydroxy-6-(p-carbethoxyphenoxymethyl)pteridine] (I). I was converted to the free acid exhibiting an ultraviolet absorption spectrum with peaks at 275 and 363 mμ, E1%1cm. 1.114 and 267, resp. Also described are the following compds. in which R = p-(2-amino-4-hydroxy-6-pteridylmethoxy)benzoyl: L-EtO2CCH(NHR)CH2CH2CO2Et, showing peaks at 258 and 366 mμ, E1%1cm. 642.5 and 177.5, resp.; L-HO2CCH(NHR)CH2CH2CO2H (oxopterin-G), having peaks at 258 and 364 mμ, E1%1cm. 855 and 185, resp.; and L-HO2CCH(NHR')CH2CH2CO2H (R' = p-(2,4-diamino-6-pteridylmethoxy)benzoyl), with peaks at 259 and 264 mμ, E1%1cm. of 599 and 166, resp. (in 0.1N NaOH)

IT 57963-55-0P, Glutamic acid, N-[p-[(2,4-diamino-6-pteridyl)methoxy]benzoyl]-, L-
RL: PREP (Preparation)
(preparation of)

RN 57963-55-0 HCAPLUS

CN L-Glutamic acid, N-[4-[(2,4-diamino-6-pteridinyl)methoxy]benzoyl]- (CA INDEX NAME)

Absolute stereochemistry.



L62 ANSWER 208 OF 215 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1953:41301 HCAPLUS Full-text

DOCUMENT NUMBER: 47:41301

ORIGINAL REFERENCE NO.: 47:6953d-g

TITLE: Cancerocidal substances. I. Effect of pterins on the Yoshida sarcoma

AUTHOR(S): Sakurai, Yoshio; Yoshino, Keishi

SOURCE: Yakugaku Zasshi (1952), 72, 1294-6
CODEN: YKKZAJ; ISSN: 0031-6903

DOCUMENT TYPE: Journal

LANGUAGE: English

ED Entered STN: 22 Apr 2001

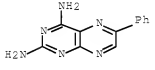
AB p-AcNHC6H4Ac is oxidized with SeO2 to p-AcNHC6H4-COCH(OH)2 (I); I.NaHSO3 gives a phenylosazone, m. 217°. 2,4,5,6-Tetraaminopyrimidine (1 g.) and 10 g. Na2SO3 in 50 ml. water poured into 20 ml. water containing 1 g. NaHSO3 and 2 g. I.NaHSO3, let stand overnight, the precipitate (0.45 g.) filtered, taken up in 10% AcOH, the solution filtered, the filtrate adjusted to pH 7, and the precipitate filtered and recrystd., yield 2,4-diamino-6-(p-acetamidophenyl)pteridine (II), which gives a neg. diazo reaction for primary amines. II (1 g.) heated 3 hrs. on a steam bath with 200 ml. 15% HCl, the solution filtered, the filtrate adjusted to pH 7 with NH4OH, and the precipitate filtered and recrystd., yields the 6-(p-H2-NC6H4) analog of II giving a red, diazo reaction with 2-naphthol. I and 4-hydroxy-2,5,6-

triaminopyrimidine give 2-amino-4-hydroxy-6-phenylpteridine, showing yellow, a green fluorescence in aqueous solution I and 2,4,5,6- tetraaminopyrimidine give 2,4-diamino-6-phenylpteridine, yellow, forming a fluorescent aqueous solution Condensation of 2,4,5,6-tetraaminopyrimidine and glucose in the presence of N2H4.H2O give 2,4-diamino-6-(D-arabo- tetrahydroxybutyl)pteridine, yellow. These as well as 2,4-diamino-4-hydroxy- and 2-amino-4-hydroxypteridine caused severe damage to the nuclei of tumor cells on intraperitoneal injection of 1 mg./kg. rat; other simpler pteridines showed no remarkable effect on animals within the dosage of 10-100 mg./kg.

IT 1026-36-4P, Pteridine, 2,4-diamino-6-phenyl- 883310-61-0P
, Pteridine, 2,4-diamino-6-D-arabo-tetrahydroxybutyl-
RL: PREP (Preparation)
(preparation of)

RN 1026-36-4 HCAPLUS

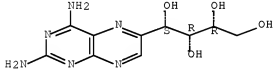
CN 2,4-Pteridinediamine, 6-phenyl- (CA INDEX NAME)



RN 883310-61-0 HCAPLUS

CN 1,2,3,4-Butanetetrol, 1-(2,4-diamino-6-pteridyl)-, D-arabo- (5CI) (CA INDEX NAME)

Relative stereochemistry.



L62 ANSWER 209 OF 215 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1953:34974 HCAPLUS Full-text

DOCUMENT NUMBER: 47:34974

ORIGINAL REFERENCE NO.: 47:5947b-d

TITLE: Pteridines. V. The mechanism of the formation of folic acid

AUTHOR(S): Sato, Hideo; Kimura, Ken

CORPORATE SOURCE: Inst. Technol., Tokyo

SOURCE: Nippon Kagaku Zasshi (1951), 72, 953-5
CODEN: NPKZAZ; ISSN: 0369-5387

DOCUMENT TYPE: Journal

LANGUAGE: Unavailable

ED Entered STN: 22 Apr 2001

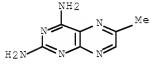
AB A crude product in the synthesis of folic acid (I) from 2,4,5-triamino-6-hydroxypyrimidine (II), CH2BrCHBrCHO (III), and N-(p-aminobenzoyl)-glutamic acid (IV), treated in dilute NaOH, with AcOH to pH 6-7 yielded a yellowish precipitate, 0.2 g. of which, purified twice by dissolving in alkali and precipitating with AcOH at pH 6.5, gave 50 mg. of a compound, C7H7ON5,

identified as 2-amino-4-hydroxy-6-methylpteridine by oxidation to the corresponding 6-carboxylic acid with KMnO4. Similarly, a by-product precipitated at pH 4-5.5 in the synthesis with (CH2Br)2CO instead of III was found to be the 7-Me isomer. III (1 g.) in 50 cc. alc. was added dropwise to 1 g. II and 1 g. IV in 100 cc. H2O, with the pH maintained at 4.0 by adding AcOH; after 15 min. the precipitate was collected, repeatedly washed with H2O and alc. One half of the precipitate (which contained Br) was stirred 8 hrs. with 1 g. IV in 50 cc. H2O, and another half with 50 cc. H2O, both at pH 4 to give 46 and 13 mg., resp. These findings indicate that III reacts first with II to give 2,4-diamino-5-(1-formyl-2- bromoethylamino)-6-hydroxypteridine which, in turn, condenses slowly with IV to yield I.

IT 708-74-7P, Pteridine, 2,4-diamino-6-methyl-
RL: PREP (Preparation)
(preparation of)

RN 708-74-7 HCAPLUS

CN 2,4-Pteridinediamine, 6-methyl- (CA INDEX NAME)




L62 ANSWER 210 OF 215 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1953:34973 HCAPLUS Full-text

DOCUMENT NUMBER: 47:34973

ORIGINAL REFERENCE NO.: 47:5946i,5947a-b

TITLE: Pteridines. IV. The formation of 6- or 7-isomers of pteridines

AUTHOR(S): Sato, Hideo; Nakajima, Michiaki; Tanaka, Hiroshi

CORPORATE SOURCE: Inst. Technol., Tokyo

SOURCE: Nippon Kagaku Zasshi (1951), 72, 868-70
CODEN: NPKZAZ; ISSN: 0369-5387

DOCUMENT TYPE: Journal

LANGUAGE: Unavailable

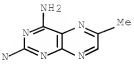
ED Entered STN: 22 Apr 2001

AB IV (1.41 g.) in 75 cc. H2O and 1.26 g. AcCHCl2 in MeOH were refluxed, with the pH kept at 1.6, to yield 250 mg. 2-amino-4-hydroxy-6-methylpteridine (X), identified by oxidizing with KMnO4 in aqueous alkali to the corresponding acid and comparing its absorption maximum (240 and 310 mμ) with those of an authentic specimen. At pH 7 the product was 100 mg. of 7-Me isomer (XI) (the absorption maximum of the corresponding acid, 377 mμ). IV and II gave X at pH 4 and, both X and XI at pH 1.6. IV and (CH2Br)2CO gave both X and XI at pH 4 and X at pH 1.6. Similarly, I with II at pH 8 gave 2,4-diamino-6-methylpteridine.

IT 708-74-7P, Pteridine, 2,4-diamino-6-methyl-
RL: PREP (Preparation)
(preparation of)

RN 708-74-7 HCAPLUS

CN 2,4-Pteridinediamine, 6-methyl- (CA INDEX NAME)



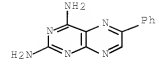
L62 ANSWER 211 OF 215 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1953:6363 HCAPLUS Full-text
DOCUMENT NUMBER: 47:6363
ORIGINAL REFERENCE NO.: 47:1136e-i,1137a-h
TITLE: Use of nitro- and halo-ketones in the synthesis of pteridines, including pteroic acid, from 2,4,5-triamino-6 hydroxypyrimidine
AUTHOR(S): King, F. E.; Spensley, P. C.
CORPORATE SOURCE: Oxford Univ., UK
SOURCE: Journal of the Chemical Society (1952) 2144-52
CODEN: JCSOA9; ISSN: 0368-1769
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
OTHER SOURCE(S): CASREACT 47:6363
ED Entered STN: 22 Apr 2001
AB cf. C.A. 44, 1116a. The bisulfite compound (I) from 2,4,5-triamino-6-hydroxypyrimidine (II) (9 g.) in 35 cc. hot H2O, treated with 15 cc. concentrated HCl, gives 4.9 g. of the di-HCl salt (III), m. above 300°. I (6 g.) in 25 cc. hot H2O, treated with 3 g. O2NCH2CH:NONa and warmed 30 min. at 50°, gives 61% 2(or 4)-5-diamino-4(or 2)-hydroxy-6-(2- nitroethylideneamino)-pyrimidine (IIIA), with 1 mol. H2O, orange-brown, m. above 300°; warm 2 N H2SO4 gives the sulfate of II; reduction of IIIA gives intractable products, but the sky-blue fluorescence of the dilute alkaline solns. indicates the partial formation of the expected 2-amino-4-hydroxypteridine. 2,4,5,6-Tetraminopyrimidine bisulfite (IV) gives no precipitate with O2NCH2CH:NOH. III (0.5 g.) and 1 g. AcONa in 5 cc. H2O, treated with 0.4 g. BzCH2NO2 in 20 cc. warm 50% aqueous EtOH, gives 70% 2,5-diamino-6-hydroxy-4-(2-nitro-1-phenylethylidene-amino)pyrimidine (V), with 1 mol. H2O, orange, m. above 300°. V (1.1 g.) in 25 cc. boiling 25% EtOH, treated during 1 hr. with 5 g. Na2S2O4 and boiled an addnl. hr., gives 2-amino-4-hydroxy-7-phenylpteridine (VI) (C.A. numbering), with 1 mol. H2O, buff, m. above 360°. I (2 g.)in 75 cc. hot 50% aqueous EtOH, treated with 1.6 g. BzCH2NO2 in 50% EtOH and refluxed 2 hrs., give 26% VI. III (0.9 g.) in 9 cc. H2O, treated with 1.8 g. AcONa and 0.6 g. BzCHO in 5 cc. 50% aqueous EtOH, gives 97% VI; sulfate, C12H9ON5.0.5H2SO4.H2O, yellow, m. above 300°; Na salt, with 1 mol. H2O, yellow, m. above 300°, intense sky-blue fluorescence in H2O. VI is largely unchanged on heating 15 min. at 200°. VI (5 g.) in 50 cc. 4 N NaOH, heated 20 hrs. at 170°, gives 20% of the Na salt (VII), decomps. about 295°, of 2-amino-6-phenylpyrazine-3-carboxylic acid, pale yellow, m. 225° (decomposition), purple-blue fluorescence; the filtrate from VII, on acidification to pH 2, gives 50% 2-hydroxy-6-phenyl-pyrazine-3-carboxylic acid, buff, m. 208-9° (decomposition); Et ester, pale yellow, m. 112°. VII (0.8 g.) in 12 cc. 80% H2SO4, heated 15 min. at 200°, yields 70% 2-amino-6-phenyl- pyrazine, m. 125-6° (cf. Weijlard, et al., C.A, 39, 30012). III and (ClCH2)2CO give 53% 2-amino-4-hydroxy-6-methyl-pteridine. III (4.5 g.) in 80 cc. 50% aqueous EtOH, treated with 13.5 g. AcONa and 3.8 g BzCHCl2 and refluxed 1.5 hrs., gives 60% 2-amino-4-hydroxy-6-phenylpteridine (VIII), with 1 mol. H2O, deep orange, m. above 360°; sulfate, with 1 mol. H2O, pale yellow, m. above 360°. VIII (3.1 g.) and 32 cc. 4 N NaOH, heated 24 hrs. at 170°, give 57% 2-hydroxy-5-phenyl-3-pyrazinecarboxylic acid, bright yellow needles or yellow prisms, m. 200°

(decomposition), brilliant pale green fluorescence; Et ester, pale yellow, m. 158-9°. The tri-HCl salt from IV (1 g.), 2.8 g. AcONa, and 0.75 g. BzCHCl2 in 10 cc. 50% EtOH, refluxed 6 hrs., give the sulfate, with 1 mol. H2O, yellow, m. above 300°, of 2,4-diamino-6- phenylpteridine, with 0.5 mol. H2O, m. 285-6°, brilliant light blue-green fluorescence. IV (2 g.) and 13 g. BzCHO in 80 cc. 50% EtOH, refluxed 15 min., give the sulfate, with 1 mol. H2O, pale yellow, m. above 300°, of 2,4-diamino-7-phenylpteridine, pale yellow, m. 290-1° (decomposition); a pure compound was not obtained from IV or the tri-HCl salt with BzCH2NO2 and Na2S2O4. p-H2NC6H4CO2H and HOCNa:C(NO2)CHO (IX) in H2O give an immediate precipitate of p-(3-hydroxy-2- nitroallylideneamino)benzoic acid (X), yellow, m. 234° (decomposition). III (0.17 g.) and 0.4 g. AcONa in 5 cc. H2O, added to X in hot 50% EtOH and heated to boiling, give 0.16 g. 2,5-diamino-6-hydroxy-4-(3-hydroxy-2- nitroallylideneamino)pyrimidine (XI), orange-yellow, m. 360°; 0.52 g. XI results from 8.6 g. III, 0.8 g. AcONa, and 0.4 g. IX in H2O. p-H2NC6H4CO2Et similarly gives the Et ester (XII) of X, yellow, m. 158-9°; 0.88 g. XII and 0.36 g. o-C6H4(NH2)2 in 20 cc. EtOH, refluxed 1 hr., give 81% 6-nitro-2,3-benzo-1,4-diazepine, deep red, m. 360°, and 61% p-H2NC6H4CO2Et; the same compound (71%) results from o-C6H4(NH2)2 and IX. OHCCHBrCHBrCO2H (XIII) (0.65 g.), 1.1 g. III, and 0.7 g. AcONa in H2O immediately give 0.85 g. 2(or 4),5-diamino-4(or 2)-(2,3-dibromo-3-carboxyallylideneamino)-6-hydroxypyrimidine, bright yellow, m. above 360°. p-H2NC6H4CO2Et (1.65 g.) and 2.6 g. XIII in 10 cc. EtOH, refluxed 20 min., diluted with 300 cc. H2O, and refluxed 1 hr. with 0.84 g. NaHCO3, give 20% Et p-(2-bromo-3- hydroxyallylideneamino)benzoate (XIV), very pale yellow, m. 159-60°; with III this yields a yellow-orange compound (not identified). C12CHCO2H (34 cc.) and 37 cc. PBr3, heated 1 hr. at 100° and then to 190°, give 81% dichloroacetyl bromide (XV), b. 125-9°. (ClCH2)2CO (20 cc.), gradually treated with 10 cc. Br on the steam bath, gives 67% 3-bromo-1, 1-dichloroacetone (XVI), b25 92-3°, m. 30-1° (semicarbazone, m. 131°); 20 g XV in ether, added (15 min.) to 8.2 g. CH2N2 in ether at room temperature, gives 23% XVI. AcCCl2CO2Et (75 g.) at 50°, treated dropwise with 20 cc. Br and heated 15 min. at 90°, gives 45% Et γ-bromo-α, α-dichloroacetoacetate (XVII), b11 127°; XVII also results (43%) by saturating BrCH2COCH2CO2Et with Cl (cooling in H2O); refluxed with H2O, XVII gives some XVI. XVI (2.06 g.), 1.82 g. p-H2NC6H4CO2Et, and 1.26 g. NaHCO3 in 8 cc. 90% EtOH, shaken 3 days, treated with 2.1 g. III and 5.3 g. AcONa in 40 cc. 50% EtOH, and the precipitate (0.9 g.) treated 2-3 hrs. (N atmospheric) with 40 cc. 2 N NaOH, give 0.4 g. of a gelatinous product having 10% pteroic acid (XVIII) activity for Streptococcus faecalis. p-H2NC6H4CO2H (1 g.), 1.5 g. III, and 6 g. AcOH in 50 cc. EtOH and 150 cc. H2O, treated with 1.5 g. XVI, give 0.3 g. product with 17% XVIII activity. p-H2NC6H4CO2H (1 g.) and 1.5 g. III in 100 cc. EtOH and 150 cc. H2O, treated with 1.5 g. XVI in 50 cc. EtOH, the pH adjusted to 4-4.3 with NaOH and stirred with a stream of N, give (1 hr.) 0.4 g. XVIII (17% activity), 0.35 g. (5 hrs.) (36% activity), and 0.07 g. (36 hrs.) (50% activity); over-all yield 9.9%. III (1.5 g.) and 1.9 g. p-aminobenzoyl-L-glutamic acid in 200 cc. 25% EtOH, treated with 1.5 g. XVI (pH at 3.25-3.55) and stirred with N, give 14% pteroylglutamic acid (0.42 g. after 0.5 hr. with 34% activity and 0.54 g. after 18 hrs. with 57% activity).

IT 1026-36-4P, Pteridine, 2,4-diamino-6-phenyl-
RL: PREP (Preparation)
(preparation of)

RN 1026-36-4 HCAPLUS

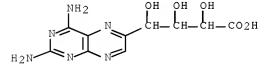
CN 2,4-Pteridinediamine, 6-phenyl- (CA INDEX NAME)



L62 ANSWER 212 OF 215 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1952:29799 HCAPLUS
DOCUMENT NUMBER: 46:29799
ORIGINAL REFERENCE NO.: 46:5094h-i,5095a
TITLE: 2,4-Diamino-6-(3-carboxy-1,2,3-trihydroxypropyl)pteridine
INVENTOR(S): Petering, Harold G.; Schmitt, John A.
PATENT ASSIGNEE(S): Upjohn Co.
DOCUMENT TYPE: Patent
LANGUAGE: Unavailable
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| US 2568462 | | 19510918 | US 1950-175478 | 19500722 <-- |

ED Entered STN: 22 Apr 2001
AB Condensation in an acid solution (pH 4.5-5.0) of 2,4,5,6-tetraaminopyrimidine (I) and 5-ketogluconic acid (II) in the presence of N2H4 (III) by heating on a steam bath yields 2,4-diamino-6-(3-carboxy-1,2,3- trihydroxypropyl)pteridine (IV). E.g., I.HCl 1.065, NaOAc.3H2O 1.36, II 2.36 (as the Ca salt), and boric acid 0.6 g. are treated with glacial HOAc 1.4, 85% III 0.6, and H2O 10 mL., and the resulting solution heated 45 min. at 85-95° (the pH of this solution is 4.5-5.0); the precipitate formed on cooling is washed with H2O twice, and once each with EtOH and Et2O, giving 1.74 g. IV, absorption maximum in 0.1 N NaOH at 257 and 370 mμ, min. at 238 and 322 mμ, E 257 mμ/370 mμ, ratio 3.1. IV is useful as an intermediate, particularly for 2,4-diamino-6-formylpteridine.
IT 36093-91-1P, 6-Pteridinebutyric acid, 2,4-diamino-α,β,γ-trihydroxy-
RL: PREP (Preparation)
(preparation of)
RN 36093-91-1 HCAPLUS
CN 6-Pteridinebutanoic acid, 2,4-diamino-α,β,γ-trihydroxy- (CA INDEX NAME)



L62 ANSWER 213 OF 215 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1952:29798 HCAPLUS
DOCUMENT NUMBER: 46:29798

ORIGINAL REFERENCE NO.: 46:5094d-h
TITLE: 2,4-Diaminopteridines
INVENTOR(S): Seeger, Doris R.
PATENT ASSIGNEE(S): American Cyanamid Co.
DOCUMENT TYPE: Patent
LANGUAGE: Unavailable
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE | |
|---|---|---|---|---|---|
| US 2568597 | | 19510918 | US | | <-- |

ED Entered STN: 22 Apr 2001

AB 2,4,5,6-Tetraaminopyrimidine (I) with CH2XCHXCHO and a primary aromatic amine, in H2O as a solvent, at 0-100° and pH 1.5-6 gives 2,4-diaminopteridines. An unexplained oxidation during the reaction gives rise to the pteridine rather than dehydropterin; better results are obtained when an oxidizing agent of -0.49 to -1.42 v. potential is added. E.g., I sulfate 2.7, and BaCl2.2H2O 2.4 are slurried 10 min. with H2O 60 at 60°, cooled to 45°, p-aminobenzoylglutamic acid 1.33 added, the pH adjusted to 3 with caustic, CH2BrCHBrCHO 2.2 in HOAc, iodine 1.3, and KI 25 in H2O 8 added, with the pH kept at 3, the mixture stirred 30 min., the slurry treated after cooling with Hyflo 1, filtered, washed with H2O and alc., a sample of crude product 2 slurried with lime 4 and H2O 2000 15 min. at 60-70°, filtered, the filtrate treated with Hyflo and 20% ZnCl2 solution to pH 10.6, clarified, heated at 80°, more ZnCl2 solution added to pH 6.8, and the Zn salt filtered with Hyflo; after treatments with lime and then MgCO3 1.1 parts N-[p-(2,4- diaminopyrimido[4,5-b]pyrazin-6-ylmethylamino)benzoyl] glutamic acid of 74.3% purity is obtained. In 0.1 N NaOH, its UV absorption maximum are at 260, 284, and 370 mμ, and min. at 239, 271, and 333 mμ. Also prepared are N-[p-(2,4-diaminopyrimido[4,5-b]pyrazin-6-ylmethylamino)benzoyl]- γ-glutamyl-γ-glutamylglutamic acid; N-[3,5-dibromo-4-(2,4- diaminopyrimido[4,5-b]pyrazin-6-yl-methylamino)benzoyl]glutamic acid; N-[p-(2,4-diaminopyrimido[4,5-b]pyrazin-6-ylmethylamino)benzoyl]aspartic acid (UV absorption in 0.1 N NaOH, maximum at 260, 282.5, and 370 mμ, min. at 237.5, 270, and 330 mμ; in 0.1 N HCl, maximum at 242.5 and 290 mμ, min. at 235 and 260 mμ); p-(2,4-diaminopyrimido[4,5-b]pyrazin-6- ylmethylamino)benzoic acid; N-(p-aminobenzoyl)alanine, m. 192.5-4° (from 60% alc.); the N-[p-(2,4-diaminopyrimido[4,5-b]-pyrazin-6- ylmethylamino)benzoyl] derivs. of alanine, valine, serine, sarcosine, and ε-aminocaproic acid. These compds. are useful in exptl. medicine as having remarkable antagonistic activity to pteroylglutamic acid. (Cf. C.A. 44, 5401a, and U.S. 2,443,163).

IT 36093-91-1P, 6-Pteridinebutyric acid, 2,4-diamino-α,β,γ-trihydroxy-
RL: PREP (Preparation)
(preparation of)

RN 36093-91-1 HCAPLUS

CN 6-Pteridinebutanoic acid, 2,4-diamino-α,β,γ-trihydroxy- (CA INDEX NAME)

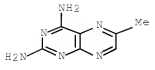
L62 ANSWER 214 OF 215 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1950:736 HCAPLUS Full-text
DOCUMENT NUMBER: 44:736
ORIGINAL REFERENCE NO.: 44:161c-i,162a-h
TITLE: Analogs of pteroylglutamic acid. III. 4-Amino derivatives
AUTHOR(S): Seeger, Doris R.; Cosulich, Donna B.; Smith, James M., Jr.; Hultquist, Martin E.
SOURCE: Journal of the American Chemical Society (1949), 71, 1753-8
CODEN: JACSAT; ISSN: 0002-7863
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
ED Entered STN: 22 Apr 2001
AB cf. C.A. 43, 3424a. 2,4,5,6-Tetraminopyrimidine sulfate-2H2O (I) (27.4 g.), 24.4 g. BaCl2.2H2O, and 500 cc. H2O were heated 10 min. at 60°, cooled to 45°, 13.3 g. N-(p-aminobenzoyl)-L(+)-glutamic acid (II) added, then 5 N NaOH to pH 3, 21.7 g. BrCH2-CHBrCHO in HOAc, and 12.5 g. iodine and 25 g. KI in H2O added simultaneously with aqueous NaOH to maintain a pH of 2.8-3.0, the mixture cooled after 20 more min. at 45° and pH 2.8-3.0, and filtered at pH 4 to give 50-60 g. crude N-{p-[(2, 4-diamino-6-pteridylmethyl) amino] benzoyl}glutamic acid ("aminopterin") (III) (method of Waller, C.A. 42, 8200f). III was also prepared from Br2CHCOCH2Br, I, and II by the method of H. and Dresibach (U.S. 2, 443, 165, C.A. 42, 7944b). Crude III (50 g.), assaying 9-12% (cf. Hutchings, et al., C.A. 41, 6595e), in 2200 cc. H2O and 10 cc. 50% NaOH at 80° was treated with 10 g. CaCl2 in H2O, the filtrate adjusted to pH 10.7 with aqueous ZnCl2, clarified, acidified to pH 4, and filtered, the precipitate in 2500 cc. dilute alkali at 80° cooled to 20°, acidified to pH 4, the filtrate acidified to pH 4, the precipitate decolorized with Darco G-60 as the Mg salt dissolved in 2000 cc. H2O, precipitated at pH 4, and the procedure repeated to give 3.9 g. III of 70-80% purity. Slurrying 3 g. III (79%) with 1.5 g. MgO and 1.5 g. Darco in 150 cc. H2O at 90 °, cooling the filtrate, and crystallizing 4 times from hot H2O gave yellow needles of C18H18O5N8Mg.3H2O, converted in H2O at pH 4 to the free acid, C19H2OO5N8.H2O. III (0.59 g. 84.7% pure) heated in 20 cc. N NaOH 6 hrs. at 100° under N, cooled, H2O added, and the pH adjusted to 3 gave 0.395 g. pteroylglutamic acid (IV) (65.5% by bioassay and 70% by ultraviolet spectra). Oxidation of 0.5 g. III in 150 cc. N NaOH with excess KMnO4 at 90-5° gave 0.177 g. 2-amino-4-hydroxy-6-pteridinecarboxylic acid (V), isolated as from VII below, showing the attachment of the side chain to the pteridine nucleus in the 6-position. Passage of O through 0.59 g. III in 20 cc. N NaOH at 100° 6 hrs. cleaved the CH2 bridge and on acidification gave 0.235 g. mixture of V and the 6-Me analog (VI), judging from the ultraviolet spectra. I (26 g.), 24 g. BaCl2.2H2O, and 700 cc. H2O were heated 10 min. at 60°, 15 g. p-MeNHC6H4CO2H added at 40° and NaOH to pH 3-4, then, at 40° simultaneously during 30 min., 21.6 g. BrCH2CHBrCHO in 21.6 cc. HOAc, 12.5 g. iodine, and 25 g. KI in 100 cc. H2O, and NaOH solution to maintain a pH of 3-4; cooling overnight and filtration with Hyflo-Supercel gave the crude p-[N-(2,4-diamino-6-pteridylmethyl)-N-methylamino]benzoic acid (VII). Heating half of the VII 40 min. at 60° in 1 l. H2O and 6 g. CaO, chilling the filtrate overnight at pH 3, heating the precipitate 10 min. at 60° in dilute NaOH at pH 11-12, filtration at 20° and pH 7, addition of dilute HCl to pH 3, cooling 16 hrs. at 5°, slurrying the precipitate in 500 cc. H2O with the min. amount of MgO to give a pH of 8.8-9.3 at 80° in 15 min., heating 15 min. more with 0.5 g. Darco, and chilling the filtrate at pH 3 (dilute HCl) gave VII of 88% purity (ultraviolet spectra). Repetition of the last step twice gave C15H15N7O2.2H2O, m. 254-5° (decomposition). The [N- (diaminopteridylmethyl)-N-methylamino]benzoyl (VIII) analog of III (A-methopterin) was similarly prepared from I and p-

MeNHC6H4CONHCH(CO2H)CH2CO2H as a yellow microcryst. product, 87% pure (ultraviolet spectra), and crystallized from very dilute HCl as C20H22N8O6.H2O, m. 185-204° (decomposition, bath preheated to 160°). No degradation products containing the 2,4-diaminopteridine nucleus were isolated, the 4-NH2 group evidently being readily converted to OH. Thus heating VII in N NaOH at 100° anaerobically 6 hrs. gave the 4-HO analog of 85% purity (ultraviolet spectra). Addition of aqueous KMnO4 to 0.5 g. VII in 166 cc. warm IV NaOH until a green color persisted after 10 min., removal of the color with NaHSO3, cooling of the filtrate at pH 3-4, centrifugation of the precipitate, solution in the min. amount of dilute NaOH, addition of solid NaOH to 5 N concentration, and chilling overnight gave a crystalline Na salt, filtered on Vinyon cloth; decolorization in H2O and addition of dilute HCl to the pale yellow filtrate to pH 3-4 precipitated 185 mg. V of 85% purity. Anaerobic heating of VIII in N NaOH at 100° gave the 4-HO analog of 85% purity (ultraviolet spectra). Addition of 25 cc. com. 30% AcCHO to 27 g. I in 2000 cc. 0.25 N HCl at 40°, then after 30 min., 130 g. of 50% NaOH and chilling gave 62.5% 2,4-diamino-7-methylpteridine (IX). KMnO4 oxidation of IX, as of VIII, acidification with dilute HCl, decolorization of the precipitate in 800 cc. of very dilute NaOH, addition of dilute HCl to pH 3.5-4.0 at 90°, and chilling gave 61% 2-amino-4-hydroxy-7- pteridinecarboxylic acid (X). Solution of 0.5 g. IX in 40 cc. H2O and the min. HCl, dilution to 80 cc. with H2O, addition of 20 cc. 5 N NaOH, then passage of a rapid stream of O at 100° 4 hrs., acidification of the yellow solution, decolorization of the precipitate in dilute NaOH at pH 11-12, and acidification precipitated 0.35 g. 7-Me analog of X. Similar anaerobic conversion was effected in N NaOH and N H2SO4. Heating 2 g. IX in 50 cc. boiling Ac2O, cooling of the red solution, and crystallization from hot EtOH after decolorization gave 0.7 g. 2,4-diacetamido-7-methylpteridine (Xa), m. 236-7°. I (26 g.) and 260 g. Na2SO3 in 900 cc. H2O were heated to 60°, cooled to 30°, and 100 cc. containing 22 cc. of 30% AcCHO and 5 g. NaHSO3 added immediately, and the yellow precipitate filtered after 40 min. at room temperature (70.5% crude yield); purification by stirring 5 g. 30 min. in 10% HOAc gave 0.475 g. insol. IX; decolorization of the yellow filtrate, addition of NH4OH to pH 6.4, and chilling 16 hrs. gave 2.2 g. 2, 4-diamino-6-methylpteridine (XI). KMnO4 oxidation of 0.5 g. XI in 166 cc. of boiling N NaOH, concentration of the filtrate at pH 3, 16 hrs.' chilling, solution of the wet centrifuged precipitate in 5 N NaOH, addition of solid NaOH to 5 N concentration, and chilling gave a crystalline di-Na salt which, decolorized in H2O and pptd with HOAc, yielded 190 mg. V. Heating 500 mg. XI with 25 cc. N NaOH under N 6 hrs. at 100° to complete solution, clarifying, and chilling at pH 4, clarifying the precipitate in the min. amount of dilute NaOH, addition of solid NaOH to 5 N concentration, and chilling gave a crystalline Na salt, which, decolorized in H2O and precipitated with HOAc, yielded 400 mg. VI. Boiling Ac2O and 1 g. XI gave 0.165 g. the 2,4-diacetamido-6-methylpteridine, m. 234.5-6.5°, marked m.p. depression with Xa. For III, the inhibition ratio for half-max, inhibition of the growth of Streptococcus faecalis R. is 1.9, 0.7, and 0.4 at pteroylglutamic acid concns. of 0.003, 0.005, and 0.01 γ/10 cc., resp. Details will be reported elsewhere.

IT 708-74-7P, Pteridine, 2,4-diamino-6-methyl-
RL: PREP (Preparation)
(preparation of)

RN 708-74-7 HCAPLUS

CN 2,4-Pteridinediamine, 6-methyl- (CA INDEX NAME)



L62 ANSWER 215 OF 215 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1947:37525 HCAPLUS Full-text
DOCUMENT NUMBER: 41:37525
ORIGINAL REFERENCE NO.: 41:7438i,7439a-b
TITLE: Growth inhibition of bacteria by synthetic pterins. I. Studies with Streptococcus faecalis, Lactobacillus casei, and Lactobacillus arabinosus
AUTHOR(S): Daniel, Louise J.; Norris, L. C.; Scott, M. L.; Heuser, G. F.
CORPORATE SOURCE: Cornell Univ., Ithaca
SOURCE: Journal of Biological Chemistry (1947), 169, 689-97
CODEN: JBCHA3; ISSN: 0021-9258
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
ED Entered STN: 22 Apr 2001
AB The following synthetic pterins were used: 2,4-diamino-6,7- dimethylpyrimido-(4,5-b)pyrazine, 2,4-diamino-7-methylpyrimido(4,5- b)pyrazine, 2,4-diamino-6,7-dicarboxypyrimido(4,5-b)pyrazine, 2,4-diamino-7-carboxypyrimido-(4,5-b)pyrazine, 2,4-diamino-6,7- diphenylpyrimido(4,5-b)pyrazine, 2,4-diaminopyrimido(4,5-b)pyrazine, 2,4-diaminophenanthro(9,10-e)pyrimido(4,5-b)pyrazine, 2,4- diaminoacenaphtho(1,2-e)pyrimido(4,5-b)pyrazine. Certain of these possess high antibacterial activity, not only for S. faecalis and L. casei which require folic acid (I) as an essential nutrient, but also for L. arabinosus, which synthesizes its own I. The substitution of OH for NH2 in the 4- or 2-position destroyed the anti-I activity. Those pterins with 4-NH2 groups varied in anti-I with the nature of the substitution in the 6- and 7-positions.
IT 716-74-5, 6-Pteridinecarboxylic acid, 2,4-diamino-
(growth inhibition of bacteria by)
RN 716-74-5 HCAPLUS
CN 6-Pteridinecarboxylic acid, 2,4-diamino- (CA INDEX NAME)

# Search History

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                SEL RN

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                OR 736919-00-9/BI OR 81827-31-8/BI OR 858127-54-5/BI OR
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L8           50 SEA SUB=L5 SSS SAM L7

     FILE 'REGISTRY' ENTERED AT 12:08:17 ON 27 DEC 2007
L9              STRUCTURE UPLOADED
L10          50 SEA SUB=L5 SSS SAM L9

     FILE 'REGISTRY' ENTERED AT 12:15:05 ON 27 DEC 2007
L11             STRUCTURE UPLOADED
L12          50 SEA SUB=L5 SSS SAM L11
L13        2708 SEA SUB=L5 SSS FUL L11

     FILE 'HCAPLUS' ENTERED AT 12:16:38 ON 27 DEC 2007
L14       16541 SEA ABB=ON  PLU=ON  L13

     FILE 'REGISTRY' ENTERED AT 14:12:21 ON 27 DEC 2007
L15             STRUCTURE UPLOADED
L16          50 SEA SUB=L5 SSS SAM L15

     FILE 'REGISTRY' ENTERED AT 14:16:43 ON 27 DEC 2007
L17       11830 SEA ABB=ON  PLU=ON  591.385.57/RID
L18           4 SEA ABB=ON  PLU=ON  L17 AND L2

ENTERED AT 14:29:57 ON 27 DEC 2007

     FILE 'REGISTRY' ENTERED AT 14:37:31 ON 27 DEC 2007
L19             STRUCTURE UPLOADED
L20          50 SEA SUB=L5 SSS SAM L19

     FILE 'REGISTRY' ENTERED AT 14:51:09 ON 27 DEC 2007
L21             STRUCTURE UPLOADED
L22          50 SEA SUB=L5 SSS SAM L21
L23        2697 SEA SSS FUL L21
L24           1 SEA ABB=ON  PLU=ON  L23 AND L2
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     FILE 'HCAPLUS' ENTERED AT 14:53:43 ON 27 DEC 2007
L25       16439 SEA ABB=ON  PLU=ON  L23

     FILE 'REGISTRY' ENTERED AT 15:02:26 ON 27 DEC 2007
L26             STRUCTURE UPLOADED
                D
L27           50 SEA SUB=L5 SSS SAM L26

     FILE 'STNGUIDE' ENTERED AT 15:03:21 ON 27 DEC 2007

     FILE 'REGISTRY' ENTERED AT 15:07:27 ON 27 DEC 2007
L28             STRUCTURE UPLOADED
L29           50 SEA SUB=L5 SSS SAM L28

     FILE 'STNGUIDE' ENTERED AT 15:08:09 ON 27 DEC 2007

     FILE 'REGISTRY' ENTERED AT 15:10:46 ON 27 DEC 2007
L30             STRUCTURE UPLOADED
L31           50 SEA SUB=L5 SSS SAM L30

     FILE 'REGISTRY' ENTERED AT 15:22:42 ON 27 DEC 2007
L32             STRUCTURE UPLOADED
L33            8 SEA SUB=L5 SSS SAM L32

L34          184 SEA SUB=L5 SSS FUL L32
L35            2 SEA ABB=ON  PLU=ON  L34 AND L2

     FILE 'HCAPLUS' ENTERED AT 15:24:46 ON 27 DEC 2007
L36          252 SEA ABB=ON  PLU=ON  L34
L37          220 SEA ABB=ON  PLU=ON  L36 AND (PRY<=2003 OR AY<=2003 OR PY<=2003)

L38            4 SEA ABB=ON  PLU=ON  DOBLHOFER R?/AU
L39           56 SEA ABB=ON  PLU=ON  TEGTMEIER F?/AU
L40           57 SEA ABB=ON  PLU=ON  (L38 OR L39)
L41            3 SEA ABB=ON  PLU=ON  L40 AND L37

     FILE 'STNGUIDE' ENTERED AT 15:26:36 ON 27 DEC 2007

     FILE 'REGISTRY' ENTERED AT 15:30:09 ON 27 DEC 2007
L42             STRUCTURE UPLOADED
L43            0 SEA SUB=L5 SSS SAM L42
L44            0 SEA SSS SAM L42
L45            7 SEA SUB=L5 SSS FUL L42

     FILE 'HCAPLUS' ENTERED AT 15:31:12 ON 27 DEC 2007
L46            9 SEA ABB=ON  PLU=ON  L45
L47            7 SEA ABB=ON  PLU=ON  L46 AND (PRY<=2003 OR AY<=2003 OR PY<=2003)

L48            2 SEA ABB=ON  PLU=ON  L40 AND L47

     FILE 'WPIX' ENTERED AT 15:32:29 ON 27 DEC 2007
L49            0 SEA SSS SAM L42
L50            1 SEA SSS FUL L42
L51            2 SEA ABB=ON  PLU=ON  L50/DCR
L52            0 SEA ABB=ON  PLU=ON  L40 AND L51

     FILE 'BEILSTEIN' ENTERED AT 15:33:24 ON 27 DEC 2007
L53            3 SEA ABB=ON  PLU=ON  L45
L54            0 SEA ABB=ON  PLU=ON  L53 AND BABSAN/FA
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     FILE 'MARPAT' ENTERED AT 15:34:31 ON 27 DEC 2007
L55             1 SEA SSS SAM L42
L56            13 SEA SSS FUL L42
L57            13 SEA ABB=ON  PLU=ON  L56/COM

     FILE 'HCAPLUS' ENTERED AT 15:36:00 ON 27 DEC 2007
L58             3 DUP REM L52 L41 L48 (2 DUPLICATES REMOVED)

     FILE 'HCAPLUS' ENTERED AT 15:36:21 ON 27 DEC 2007
                 D QUE L47
L59             5 SEA ABB=ON  PLU=ON  L47 NOT (L41 OR L48)

     FILE 'WPIX' ENTERED AT 15:36:48 ON 27 DEC 2007
                 D QUE L51
L60             2 SEA ABB=ON  PLU=ON  L51 NOT L52

     FILE 'HCAPLUS, WPIX, BEILSTEIN, MARPAT' ENTERED AT 15:37:44 ON 27 DEC 2007
L61            20 DUP REM L59 L60 L53 L57 (3 DUPLICATES REMOVED)

     FILE 'HCAPLUS' ENTERED AT 15:40:03 ON 27 DEC 2007
                 D QUE L37
L62           215 SEA ABB=ON  PLU=ON  L37 NOT (L41 OR L48 OR L47)
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